T. Wilson Smith.
Bath. 1898.

RHEUMATOID ARTHRITIS:

ITS PATHOLOGY, MORBID ANATOMY,

AND

TREATMENT.

BY

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PREFACE TO SECOND EDITION.

In response to many suggestions I now give my more matured ideas as to the nature and origin of Rheumatoid Arthritis, and it will be noticed that further experience and observation have led me, as well as others, to believe yet more firmly in the bacterial theory as to the origin of the disorder, and have also caused me to conclude that there are at least two separate forms of disease at present classed under the term rheumatoid arthritis—the one acute and undoubtedly microbic in character, the other chronic and probably degenerative. As far as possible I have tried to point out the clinical differences, so that those called upon to treat either condition may appreciate fully the requisite essentials and indications necessary to insure a successful result.

Bath, *April*, 1898.

PREFACE TO FIRST EDITION.

The writing of a treatise on Rheumatoid Arthritis involves much labour, not only on account of the mass of literature which has to be traced and classified, but, also, and more especially in my case, from the recent discovery of micro-organisms, implying, in consequence, the rewriting of all its pathology, morbid anatomy, and treatment. Such an upheaval cannot be accomplished in a day, and this small work is only intended to be an introduction to further and more perfect investigation. Many parts of it will, probably, in the near future require revision, but it has been my ambition to avoid, as far as possible, making any statement unsupported by facts or by logical deductions therefrom. I have here utilized the discovery of Dr. Wohlmann and myself of the micro-organisms which we believe to be specific to the disease, and the latter's life history and peculiarities, as worked out and elucidated by Dr. Blaxall. To them both my sincere thanks are due. In the light of our discovery I have been

led to enquire into the nature of two complaints which have been hitherto classed as only variations of one and the same disorder. This, for reasons given later on, I do not consider to be correct, and I propose to study and keep distinct Senile Arthritis from the more generalized disease Rheumatoid Arthritis.

Bath, 1896.

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ERRATA.

Page 37, line 11, for "Oster" read "*Osler.*"

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RHEUMATOID ARTHRITIS:

Its Pathology, Morbid Anatomy, and Treatment.

CHAPTER I.

INTRODUCTORY AND HISTORICAL.

Nomenclature—Evidence of its Antiquity—Landré Beauvais—Heberden—Haygarth—Cruveilhier—Adams—Fuller—Charcot—Deville—Broca—Key—Senator—Garrod—Virchow—Hutchinson—Spender—Its Individuality—Its Frequency, etc.

HITHERTO, the disease which we call Rheumatoid Arthritis has not only been known by different names, but different diseases have been classed under this heading—the number and diversity of the terms employed corresponding in a certain sense with the number and diversity of the views advanced with regard to its etiology and pathology. It is undoubtedly a disease *per se*, and has probably existed as such as far back as any other known form of disease, but it was not until the beginning of this century, or the end of the last, that it came to be recognised and differentiated from the allied disorders, gout and rheumatism. Indeed, I am not certain that in some countries it is even yet recognised as a separate form of disease, for in France and Germany some still hold it to be only a form of chronic rheumatism. This is curious, as one of the best works ever written on the subject was penned by that great observer, Charcot. Much of the difficulty surrounding the disorder is, I am sure, caused by the ambiguity of

the various terms which have, at one time or another, been applied to it, none of which seem exactly to describe its characteristics, but leave much to the imagination of the individual observer. Of recent years the principal terms employed to designate it have been those of **rheumatoid arthritis**, and **osteo-arthritis**. Now how much better would it be had we been content with one name only, even if that one did not actually describe the condition with perfect accuracy? What an amount of confusion might have been saved! This want of exactitude in nomenclature would soon have been compensated for by the increased knowledge which we would have been enabled to store up and note for comparison about a complaint, the study of which, and the disentanglement of whose literature and prevailing impressions, are enough to appal even the boldest. Many and various are the theories which, at one time or another, have been advanced to explain the congeries of symptoms called rheumatoid arthritis; and many and various are the diseases which, at one time or another, have come under our notice labelled rheumatoid arthritis, osteo-arthritis, rheumatic gout, etc., these terms being, as a rule, quite indiscriminately apportioned. No wonder confusion has reigned supreme. It is, therefore, with fear and trembling that I now endeavour, as far as our still limited knowledge renders possible, to throw a ray of light into the obscurity surrounding the etiology and pathology of the disease, with the hope that it will, in the near future, enable us to walk with surer footsteps.

Of the many names used to designate the acute or destructive form of the disorder, I have here assumed that that of **rheumatoid arthritis** is the one best known to the largest number, and, therefore, the one best suited to be used permanently. It, in my opinion, is the one fulfilling to the greatest extent the requirements of

science. This term was first applied by **Garrod**, and although it hardly gives one the best mental idea of what the disease is, yet I think, from many points of view, it is the most suitable. It has been objected that the word Rheumatoid, which means, freely translated, like rheumatism, is misleading; so it is, to a certain extent. Yet no one will deny that while quite separate and distinct, it, to a certain extent, in outward appearance at least, does resemble some forms of rheumatism. It is a much more suitable term than any of those which include Rheumatic as part and parcel of their being. Rheumatic applies to a totally different condition, and to bring it in leads to endless confusion. **Osteo-arthritis** is a term implying a condition much more marked in the chronic forms of the disease, and which I would keep for those chronic osteo-sclerotic cases so often seen in the later stages. Some have objected to the use of arthritis at all, as they hold that the inflammatory changes in the joints are merely secondary to nutritional changes elsewhere; were it not for this, the term most commonly used in Germany, **arthritis deformans**, would have become much more popular. This objection to arthritis can hardly be sustained, especially in consequence of our newer light on the origin of the disease. The late Dr. Brabazon suggested **pernicious arthritis** as a suitable term, while the French occasionally now use the expression, **rhumatisme chronique infectieux.** Both these really describe the condition better than most of the others, but as the term **rheumatoid arthritis** is distinctive, I see no really urgent reason why we should adopt a new term, which is bound to lead only to renewed confusion and to provide yet another term for our already overcrowded nomenclature.

The following is a list of the terms which have, at one time or another, been applied to the disease: —

1. "Goutte Asthenique Primitif," by Landré Beauvais, in 1800.[1]

2. "Digitorum Nodi," by Heberden, in 1804.[2]

3. "Nodosity of the Joints," by Haygarth, in 1805.[3]

4. "Chronic Rheumatism of the Joints," by Todd, in 1843.[4]

5. "Arthrite Sèche," by Deville and Broca, in 1848 and 1850.[5 and 6]

6. "Rheumatic Gout," by Fuller, in 1852.[7]

7. "Rhumatisme Chronique Primitif," by Charcot and Vidal, in 1853 and 1855.[8]

8. "Usure des Cartilages Articulaire," by Cruveilhier in 1858.[9]

9. "Chronic Rheumatic Arthritis," by Adams, in 1857.[10]

10. "Rhumatisme Noueux," by Trousseau, in 1860.[11]

11. "Arthritis Deformans," by Virchow, in 1869.[12]

12. "Rheumatoid Arthritis," by Garrod (Sir A.), in 1876.[13]

13. "Osteo-arthritis," by Spender, in 1888.[14]

14. "Pernicious Arthritis," by Brabazon, in 1896.[15]

15. "Rhumatisme Chronique Infectieux," by Chauffard and Ramond, in 1896.[16]

From this list we see that, even from the beginning, there has been a difference of opinion as to what is, and what is not rheumatoid arthritis, as well as an uncertainty as to the nature of the morbid process; some ascribing the changes to rheumatism, whereas others have thought they were gouty in nature; some, in their writings, describing typically rheumatoid cases, and others as typically what are not rheumatoid.

Turning to the history of the complaint, we find its characteristic changes have been found in the bones of its victims in times which, if not quite prehistoric, are practically so. As far as I can learn, the oldest bones

showing these changes are those found by Mr. Page May[72] in Egypt, then those found in lower Egypt by Mr. Petrie,[17] who suggests as a probable date 1300 B.C. Next come those discovered by Mr. Eve,[18] also in Egypt, and probably referable to the Ptolemaic period (second century B.C.); and following on these are those of a Norse Viking, found in the Christiania Fjord; those found in Pompeii, by Chiaje[19]; those in the Convent of Marienthon in Pomerania, by Virchow[20]; those in the Roman Sarcophagus at Smithfield, by Dr. Norman Moore[21]; those in the Catacombs of Paris, found by Lebert[22]; all showing distinct traces of bony rheumatoid, or osteo-arthritic change. Coming down to more recent times, we find the disease was first described by Sydenham,[23] from a clinical point of view, in the year 1683, as a modification of rheumatism. In 1703 it is referred to in the writings of Musgrave[24]; in 1764 and 1768 in those of Haller[25] and De Sauvages,[26] respectively. In those writings one can trace references to the disease, but it was not actually described as a disease *per se* until the year 1800, when Landré Beauvais[27] published his Thesis on "Goutte Asthenique Primitif," which condition we now recognise as one of rheumatoid arthritis. Amongst the other features to which he drew attention was the special liability of women to its attacks, its chronic nature, its destruction of the cartilages, and its enlargement and deformity of the affected joints. He recognised that it could not be due to gout, thus differentiating for the first time between that disease and rheumatoid arthritis. In 1804 Beauvais' opinion received the support of Heberden,[28] who, however, went further, and differentiated between it and rheumatism. He mentioned that there was little or no fever, no redness of the skin, no great pain, but swelling of the affected part; that the

disease was not particularly apt to begin in the foot, but if so, it soon left it and attacked other joints, several of which, one after the other, became the seat of the distemper after the first onset; that it was very crippling; and that one attack caused more weakness of the limbs than would have been produced by gout in many years. He mentioned that the wrists and the fingers were specially liable to the disease, and that once attacked it tended to remain permanently in these joints. He also described what have ever since been known as Heberden's nodes, as occurring on the terminal phalanges of the fingers.

In 1805 Haygarth [29] published his clinical "History of Diseases," which gives the clinical appearance of rheumatoid arthritis, describing it fully, and also differentiating between it and rheumatism. In 1813 Chomel [30] alluded to Landré Beauvais' thesis, but believed that the disease referred to by the latter belonged to a rheumatic type. In 1827 Scudamore [31] mentioned that he had seldom seen such cases as are described by Haygarth, except secondary to gout and rheumatism. In 1833 Brodie,[32] in his work on "Diseases of the Joints," called attention to its being quite distinct from both rheumatism and gout; and during the years 1829 to 1840 Cruveilhier [33] wrote mentioning the necessity of observing its clinical characteristics, and gave it the name, "Usure des cartilages articulaire." He pointed out that true bony ankylosis may occur. During this period also it was studied and commented upon by Lobstein [34] (1833), Key [35] (1833), Robert Smith [36] (1835), Canton [37] (1848), Deville [38] (1848), Broca [39] (1850), and Adams [40] (1857) in this country and France; whilst in Germany, Meyer [41] (1849), Weber [42] (1858), and Leis [43] wrote explaining the rationale of the various phenomena observed. These observations were subsequently con-

firmed by Cornil,[44] Vergely[45] (1858), and Ranvier[46] (1865). Deville and Broca gave it the name "Arthrite Sèche," and Adams that of "Chronic Rheumatic Arthritis." Robert Smith and Adams both pointed out that many cases of disease of the hip joint, resulting from injury, were of the nature of rheumatoid arthritis, and thereby have caused confusion with regard to the difference between it and malum coxæ senile. Adams gave many beautiful illustrations of the morbid anatomy. He said Sandifort,[47] of Leyden, was the first to notice the disease, in the hip joint, in the *post mortem* room. Adams also corroborated Cruveilhier's observation about the occurrence of true bony ankylosis, and he mentioned that the polyarticular cases were usually preceded by acute rheumatism. Moreover, he drew attention to the relationship between the monarticular cases and injury. Colles, in 1839—1857, remarked that two different processes were at work, one absorbing, and one forming fresh bone. In 1843 Todd[48] called it "Chronic Rheumatism of the Joints," and considered the changes to be more of an irritative than inflammatory nature. In 1849 Redfern[49] gave some good illustrations of the disease, and showed the nature of the cartilaginous changes. In 1852 Fuller,[50] in his work on "Rheumatism and Allied Disorders," called it "Rheumatic Gout." He said that although it was in some respects closely allied to rheumatism, yet he considered it more of a gouty nature; at the same time he thought it was not a compound of the two disorders, but a distinct disease. In 1853 Charcot and Trastour[51] published their thesis. As Charcot's views have been more largely received and criticised than any other, his opinions will come under consideration later on, and as they crop up. In 1855 Vidal[52] followed Charcot with his thesis. They all three gave it the name "Rhumatisme Chronique

Primitif," and they all held that it was only a form of chronic rheumatism. This view is still held in France by many, as may be seen from Charcot's later writings, and also from those of Besnier,[53] Homolle,[54] Lacaze-Dori,[55] and Mathieu.[56] In England, America, and Germany, this is not the view held by most writers on the subject, many of them being of the opinion that Heberden and Haygarth were right in regarding it as a disease *per se*, and that although it presents many outward appearances resembling both gout and rheumatism, yet it differs entirely in essentials, and that it is evidently a distinct disorder. Adams and Fuller, who did much work in the elucidation of the characteristics of the disease, held this view, and coming down to more recent times we find that Sir A. Garrod [57] showed unmistakably that the excess of uric acid, present in gout, was entirely absent in rheumatoid arthritis. It was classed by him under three headings, namely, acute, chronic, and irregular. The chronic form he further subdivided into general and local. Since then many have written on the subject, and their studies have brought about a profound change in the prevailing views as to its nature. Senator [58] described it under the name of "Arthritis Deformans," a name which had previously been given to it by Virchow,[59] and he believed that it was a true constitutional disease. Hutchinson [60] looked on it as the result of a rheumatic diathesis, caused by the blending of the elements of gout and rheumatism, now the one and now the other element predominating. In 1884 Sir Dyce Duckworth [61] gave it the name of "Chronic Rheumatic Arthritis," and thought it was a form of true rheumatism. Lane [62] (A.), in 1884, thought that the changes in the joints were caused simply by wear and tear; and Ord,[63] in 1885, considered it to be purely of reflex nervous origin. Spender,[64] in 1888, pointed out

some of the early nerve phenomena under the name of osteo-arthritis. In 1890 Dr. A. E. Garrod,[65] calling it "Rheumatoid Arthritis," wrote a treatise on the subject; also in that year Lane (H.) and Griffiths [66] pointed out the differences between rheumatoid arthritis, chronic rheumatic arthritis, and osteo-arthritis; while in 1893 Forsbrooke [67] brought out his dissertation, and advanced the view that it was anæmia to which it and all the vaso-motor and trophic changes were due; the joint changes he considered being due to trophic malnutrition; and quite recently Dr. Brabazon [15] suggested that it might be called "Pernicious Arthritis," referring more especially to the symptoms. In May, 1896, Chauffard and Ramond [16] drew attention to the occurrence of enlarged glands in certain cases, and also recorded the fact that in one case they succeeded in finding a small diplo-bacillus in the synovia. This diplo-bacillus differs from the micro-organisms found by Schüller,[68] but in many respects closely resembles those previously found by Dr. Wohlmann and myself.[69] In 1897, Prof. Bäumler opened a discussion on the disease at the Berlin Congress for Internal Medicine,[70] and the following conclusions were arrived at: (1,) That the name "Rheumatism" should be limited to acute rheumatism and certain variations of that disease; (2,) That a special form of disease, of poly-articular nature, distinguished by its chronic course, by having no tendency to heart disease, by not being readily influenced by the salicylic preparations, but one which quickly leads to malformations, and ultimately to destruction of the joint tissues, should be called **arthritis**, or better, **poly-arthritis deformans**; (3,) That the cause of the disease is not known with certainty inasmuch as many conditions predispose to it, such as insufficient food, nerve exhaustion, and other previous joint affections, there being also a special tendency to the

disease in women, and apparently in connection with their sexual organs. It is not more common in the poor than in the rich; (4,) That no special connection with organic or functional nerve disorders, either of a central or reflex origin, can be established; (5,) That it is not unlikely, and the more recent bacteriological researches give this idea a certain basis, that we are dealing with an infective disease; and (6,) That it should not be lost sight of that there may be several causes and infections at work at one and the same time. At the British Medical Association Meeting in Montreal, in August, 1897, Prof. Stewart [71] opened a discussion on the disease, but more especially with reference to the relationship between it and diseases of the nervous system, tuberculosis and rheumatism. Little new knowledge was brought forward, but the infective nature of the disease seemed to be gaining ground and to be generally accepted as best explaining the various phenomena of the disease.

Such are the main points in the history of the disease, and one wonders that, with such a mass of literature having direct bearing on the subject, we should have been so long in the dark, both with regard to its pathology and its etiology, and, I am sorry to say, also with regard to its morbid anatomy. Yet such is the case. If it is granted that we are dealing with a disease by itself, one would look for some salient symptom or symptoms, without which we would have no rheumatoid arthritis. This we find in the joints and nervous system. The joint symptoms are always the primary ones, the nerve phenomena being purely secondary, but their presence, in one shape or another, is so persistent that one can regard them as essential elements only. The conjunction of symptoms is such as we find in no other morbid process. It is not merely occasional joint troubles, associated with nerve lesions, or *vice versâ*, but

it is a constant conjunction of certain symptoms, in a well marked sequence, referable on the one hand to the joints, and on the other to the nervous system. We are therefore forced to the inevitable conclusion, that we are dealing with a disease *per se*, and one in which the primary lesion is in the joints.

Turning to the frequency with which it is met, I may say that it is a common form of disease occurring, as one observer states (Haygarth), as often as 1 in every 310 patients, giving a percentage of 0·32. During the years 1893 to 1897 there were admitted to the Bath Royal Mineral Water Hospital 4,744 patients, of whom 1,061 suffered from rheumatoid arthritis, 2,470 from rheumatism, and 602 from gout. It is more common in the poor and badly nourished, and is also more common in the cold damp parts of the globe than in either the dry cold or hot damp.

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CHAPTER II.

ETIOLOGY AND PATHOLOGY.

Micro-organisms a Cause—Charcot—French Views—Pye-Smith—Hutchinson—Forsbrooke—Trophic Impulses—Motor Cells—Neuritis—Reflex Action—Functional Depression—Toxic Action—Joint Changes in Tabes—Stewart—Bäumler—Muscular Atrophy—Bacteria a Cause—Arguments in Favour of this Theory—Nerve Symptoms—Chvostek's Views—Selective Actions—Primary and Secondary Symptoms—Toxæmia—Motor-ganglion Cells—Reaction of Degeneration—Muscular Atrophy—Pigmentation—Anæmia—Predisposing causes, etc.

Part I.

From the discovery made by Dr. Wohlmann and myself, no doubt remains, in my mind, that rheumatoid arthritis is caused by the micro-organisms which we found to exist in the joint fluids and tissues, and which we therefore look upon as specific. Unfortunately we have not succeeded in proving beyond cavil that these micro-organisms are the cause *par excellence*, as we have failed to reproduce the disease in animals. This remark applies also to the micro-organisms found by Schüller,[1] and Ramond and Chauffard.[2] Whether our failure arises from the insusceptibility of the animals experimented on, or from some failure in technique, I cannot say: yet the fact remains that we have not reproduced the disease, and therefore it devolves on us to bring forward such other evidence as bears on the subject, so that an unbiassed opinion may be formed as to the probability of the disease being an infective process, and as to the probability of our bacillus being the specific

cause. To clear the ground, I will state and shortly criticise such theories as have been advanced from time to time as to its pathology.

i.—According to **Charcot**, and many foreign observers, rheumatoid arthritis is only a secondary form of rheumatism, but as, in the majority of cases, the disease arises as a primary one, there can be no ground for this belief. It, undoubtedly, may arise as a sequela of acute rheumatism, or in fact of any acute arthritis; but to say it is only a form of rheumatism is, I think, grossly misrepresenting the disease and its characteristics. One has only to look at its clinical characters, quite apart from its morbid anatomy, to perceive the difference. In this country it has always been regarded as a disease *per se*, at least ever since its peculiarities were thoroughly appreciated, and, I think, it is hardly necessary for me here to point out each individual difference, but will take it for granted that, in this country at least, this individuality is admitted.

ii.—**Dr. Pye Smith** [3] holds that the disease is of a senile character. This is not often the case in true rheumatoid, and something more than **senility** must exist, in the acute cases, as they mostly arise in the young or comparatively young. It is probable that Dr. Pye Smith referred to certain cases which I class as Senile Arthritis, a disorder which I regard as purely degenerative and altogether different from the acute and specific disease we are now studying.

iii.—**Hutchinson** [4] looks upon it as simply a result of the combined action of the rheumatic and gouty processes, now the one and now the other element predominating. He believes in a **basic Rheumatic diathesis**, capable of subdivision into off-shoots. In many ways such a theory is supported by facts; but we must regard this basic diathesis as only a diathesis. The poison of gout is as

different from that of rheumatism as they are both from that of rheumatoid arthritis. It is positively certain, however, that a certain form of diathesis does predispose to arthritic changes, but what these changes will be will probably depend on local conditions.

iv.—**Forsbrooke**[5] holds that the anæmia, which is present in this disease, is responsible for the joint and other changes. He states that at first, owing to a deficiency of oxygen in the blood, the vaso-motor centre in the medulla is stimulated, and by consequent constriction of the minute vessels supplying the joints and smaller nerves, the nutrition of these parts is interfered with. This deprivation of blood, which although at first functional in nature, may give rise to organic change. The stimulation of the vaso-motor centre, if prolonged, ends in exhaustion, followed by dilatation of the joint vessels and inflammation. Ingenious as this theory is, it rests on the assumption that anæmia is present before any of the joint or nerve troubles. This has not been found to be the case, so how can it be the cause? Personally, although I have noticed anæmia in a large proportion of cases, it has not been invariably present, and it has certainly not been the first symptom. It is more likely that the anæmia is caused by the poison generating the disease; and is therefore only a sequela, not a cause. The anæmia of rheumatoid arthritis has all the characteristics of a toxæmic anæmia, and is more fully considered elsewhere.

v.—**Remak,**[6] **Senator,**[7] **Ord,**[8] **Sir Dyce Duckworth,**[9] and many others, have all been of the opinion that the disease is due to some abnormal nerve condition, although they differ as to its being a primary lesion of the nervous system, or only secondary to a lesion elsewhere. The majority hold that it originates through abnormal trophic impulses, and probably in a similar

manner to the joint changes arising in tabes dorsalis, syringo-myelia, etc. The abnormal trophic impulses are usually stated to arise from changes in the spinal cord, but it appears to me this theory is based on quite insufficient grounds, and it is difficult to see how it became so generally accepted. If we examine it, two questions arise (1,) Have any gross or other lesions sufficient to account for the abnormal impulses been found? and (2,) Can trophic impulses produce such changes as we find in this disease?

(1,) What are the conditions which might give rise to the abnormal trophic impulses?

We would expect to find some gross lesion either in the central nervous system (*a*), or in the peripheral nerves (*b*); or else some reflex (*c*), nutritional (*d*) or toxic (*e*) condition might exist which could give rise to the necessary abnormal impulses.

(a,) If due to a gross change in the central nervous system the lesion will, of necessity, be so extensive that we can think of no condition which could possibly give rise to it, unless it be a blood one. A poison circulating in the blood is the most likely agent to affect the extensive area necessarily involved: for we must remember that the trophic influences which govern the nutrition of the joints, bones, and skin are under the control of the cord, the centre being probably situated in the intermediate grey matter, whilst that of the muscles is controlled by the anterior grey matter (probably the motor nerve cells). As the nerve endings have a structural continuity with the tissues, the nutrition of the tissue molecules depends on the nutritional condition of the nerve and nerve centres. So far no gross organic change has been detected in the central nervous system, except in three cases in which Folli [10] discovered an atrophic condition in the cells of the anterior cornua. Klippel,[11]

according to Massolongo, observed somewhat similar changes, and in one case I have also observed alterations in the condition of the ganglion cells. These conditions are, however, so altogether inextensive, and have been entirely confined to the motor ganglion cells, that one must reject the idea that they can originate such a widespread disorder.

(b,) If due to a gross lesion in the nerves themselves we would expect to find symptoms of nerve degeneration in all and every case of rheumatoid disease—but this is not the case. In only a certain number is an unmistakable neuritis present, and this so often markedly follows the arthritis that there can be no doubt it is secondary in its nature. This neuritis may be caused by the existing joint inflammatory process, or else it may be due to the action of toxins circulating in the blood. It is undoubted that toxins may thus give rise to such a condition, thereby showing not only a selective action in the parts acted on, but also a peculiarity in the acting virus. MM. Pitrès and Vailliard [12] have found a well-marked neuritis in several cases, and they believe that there is a distinct relationship between the presence of this neuritis and the development of the trophic changes. It must be noted that although finding marked changes in the nerves supplying the wasted muscles yet they found none in those supplying the articulations. On the other hand Duplay and Cazin [13] found an inflammatory condition of the nerves supplying the affected joints. As will be seen, the results of such examinations have hitherto been so uncertain and contradictory that one must assume there is no constant occurrence of a neuritis. This agrees well with all clinical experience, and with what one would expect from the nature of the disease.

(c,) Dr. Ord's [14] view of the disease is that it is entirely

caused by **reflex action** set up by some uterine or other visceral derangement. He believes that the irritation engendered in the uterus causes impulses to be conveyed to the central nervous system, which in turn give rise to other morbid impulses which are conveyed, by the peripheral nerves, to the joints, etc., and there cause the changes which we know by the name of rheumatoid arthritis. Admitting that reflex influences may cause trophic changes in the skin and muscles, and apart from the fact that the disease occurs in men free from genital irritation in a proportion of one to eight women, one cannot believe that the acute organic changes in the joints can be set up by any such reflex action. Trophic lesions have been traced to injuries of the nerve centres, and of the nerves leading to the part, but not to reflex irritation, and there is no evidence that reflex irritation can give rise to such lesions of the nerves or nerve centres. Although denying that such impulses can cause organic mischief, yet I admit that, by causing debility and anæmia, they may so lessen the natural defences of the joints that these may readily become the prey of the poison, which causes rheumatoid disease. They must therefore be borne in mind as potent predisposing causes.

(d,) Is this disease then, as we cannot explain it otherwise, due to a **functional depression** of certain areas of the cord or of some of the peripheral nerves? It is possible to conceive that deficient nutrition of certain areas might set up trophic changes, and as this condition is likely to occur in all debilitating states we would look for it as a sequela of acute illness, or else in those who are congenitally weak. Dr. Garrod[15] states that out of 500 cases of rheumatoid arthritis he traced a family history of arthritic trouble in 216. Rheumatoid disease practically only occurs in debilitated people, and is often a

sequela of some acute condition which has left impairment or enfeeblement of the nutritional state, both of the body generally and of the nervous system locally. This, however, may be said of any disease, and is only therefore of negative value; what is of more importance is the fact that it would be against all experience to find permanent symptoms, such as are seen in this disease, arise without some slight change in the ultimate nerve elements, which might be recognisable on microscopic examination. If due to nutritional changes we would look for some alteration in the medulla as being that portion of the motor path which has the least nutritional stability. Could we explain the joint symptoms by other means, we might readily conceive how nutritional changes might be set up which would account for the trophic and vaso-motor symptoms.

(c,) With regard to the **toxic** action of **bacterial poisons** on the nervous system, it is of importance to note that nutritional, as well as actual organic change may result. The nerves under these circumstances are usually more liable to be affected than the spinal cord; but there are many diseases in which it is obvious that it is the central nerve centres which are affected, as for example in syphilis, tetanus, etc. Toxic agents, however, often exhibit a remarkable selective action, and as yet we do not know what are the influences which determine such susceptibility. For example, take the case of alcohol, which being itself the result of the growth of organisms, and being almost as low in the scale as the bacterial toxic agents, gives rise to many and diverse nerve conditions. Again the question arises, Can it be possible that the action of toxic products is limited to certain cells or groups of cells? Buzzard[16] says there are reasons for believing that this is quite possible, and as instances he quotes various epidemics of infantile and

spinal paralysis which it is impossible to doubt were due to an infective origin. To admit the action of toxic poisons on the nerve system and exclude that of their originators on the local joint structures would be illogical.

(2,) Apart from the question of finding gross lesions the question is, Can trophic abnormal impulses produce such lesions as we find in the diseased joints? I hold that they cannot. They can, and undoubtedly do, produce muscle, integumentary, and other nutritional changes. But that they can bring about such acute conditions as exist in rheumatoid arthritis I cannot believe. In tabes the joint changes are altogether different in nature and appearance, and depend on a definite nerve lesion. In syringo-myelia they are also different. In ataxic paraplegia, and many other forms of nerve disease, we also see arthritic changes, but, on the one hand, they are all accompanied by definite nerve lesions, and on the other they seldom present more than swelling, and effusion into the joint. A wasting, with some slight reparative change, one might possibly get; but it appears to me inconceivable that such extensive inflammatory lesions could arise without some sure and certain guide to a nerve lesion, easily recognisable on either macro- or microscopic examination. Marie,[17 and 18] one of our most accurate observers, says the pathological anatomy of tabes and rheumatoid arthritis is quite distinct, and that although points of difference might be mentioned, in his eyes this is not necessary. But let us study this point more carefully. As has been said, in tabes, syringo-myelia, progressive muscular atrophy, hemiplegia, ataxic paraplegia, etc., we occasionally find arthritic lesions, and, as a type, let us take tabes. In this disease we may have arthritic changes either of an atrophic or hypertrophic form, or a mixture

of both forms may occur. The joint changes usually appear suddenly with no pain and affect chiefly the larger joints, such as the knee, and are characterized by effusion into the synovial sac followed by destruction of the cartilages and general disorganisation of all the joint structures. The bones may waste, or bony out-growths may appear. Such are the clinical features as seen in nerve arthropathies, and it will be noticed that they differ very considerably from what we see in rheumatoid arthritis. Two theories have been advanced as to the occurrence of these changes, neither of which exactly fits the case of rheumatoid arthritis. One is, that the function of the so-called trophic centres for the joints in the cord is interfered with, thereby implying some central lesion; the other, which is probably the true one, is that owing to lessened or disturbed sensation traumatic influences, which pass unnoticed, set up the inflammatory joint changes. It is obvious that in rheumatoid arthritis we have neither central nerve lesions nor have we a disturbance of sensation. Stewart,[19] speaking on the subject, says there are very strong grounds for believing that the joint changes in rheumatoid disease are not due to disease in the spinal cord, as should such changes be brought about in that way we would expect some evidence on examination of these changes in the cord. The strong presumption is therefore that the joint changes do not arise in consequence of a nerve lesion.

Having thus disposed of the more common views, let us now consider some other arguments which have, from time to time, been advanced to prove that rheumatoid arthritis is due to a nerve disorder. We find Dr. Garrod[20] quoting several cases where the disease developed after a shock to the nervous system. As Bäumler[21] says, this can only be regarded as pre-disposing and not as the

exciting cause. Again, Dr. Spender [22] mentions various nerve phenomena which he has noticed occurring soon after the onset of the joint lesions. He mentions such symptoms as pigmentation of the skin, local sweatings, neuralgia, tachycardia, etc. He also mentions cases where "bulbar warnings" were noticed quite early in the disease, [22 and 23] and which progressed only to terminate with the death of the patient. He maintains that the arthritis is not the cause of muscular atrophy, and that which is called "arthritic muscular atrophy" does not arise in a similar way to that of rheumatoid arthritis. He says the muscular atrophy of rheumatic arthritis is a reflex tropho-neurosis, a pure irritation of the articular nerves, causing atrophy through the anterior cornua of the cord, whilst that of rheumatoid arthritis is an integral part of the disease, and the cause of the arthritis is the cause of the atrophy. The most difficult point to explain in rheumatoid arthritis is certainly this **muscular atrophy.** It is one of the most important and earliest symptoms, and is usually, from the very first, well marked. It extends to the whole of a muscle, and not only to that part which is in contact with the joint, or distal to it; and it follows so closely on the first appearance of the joint-trouble as to preclude the possibility of extension of inflammation to the nerves. It is found that the extensors are principally affected, but not exclusively so. The selective character of the atrophy is a sufficient proof that the changes in the muscles cannot be set down to mere disuse. It has usually been attributed to some reflex nerve influence having its origin in the peripheral nerves of the affected joints. This has been suggested by Paget, Vulpian,[24] Charcot, and others. They argue that, assuming a derangement in the nutrition of the motor cells of the cord, determined by the morbid impulses from the joint-

nerves, the influences from the motor cells will, in all probability, determine the alterations in the muscle nutrition. This theory, they hold, is supported by the fact that by the previous division of the posterior spinal roots,[25 and 26] wasting of the muscles can be prevented in arthritis of the knee-joint artificially produced. Such an argument cannot be admitted to apply to the atrophy of rheumatoid arthritis, the one being an experimental arthritis in a healthy animal, the other being the evidence of a diseased condition. It is known that disease in a joint may set up spinal trouble,[27] *e.g.*, primary spastic paraplegia, and from this we gather that influences from the joint nerves act on the controlling structure of the muscle reflex centre. The muscle reflex centres seem also to be under the influence of other centres, because if there be disease higher up they may also pass into a condition of increased activity, the path which determines their activity being the pyramidal tract. At the same time, we must remember that atrophy takes place in all forms of chronic arthritis and even in subacute cases such as are seen in syphilitic, tuberculous, or hæmophylic disease. No matter what the cause is then, the first lesion is in the joints, and not in the spinal cord. Another theory is that the atrophy is caused by reflex vaso-motor spasm: this view was advanced by Brown-Séquard; whilst Strümpell [28] suggested that the inflammation might have spread from the joints to the muscles, setting up a myositis; and in one class of cases it has been noted by Sabourin [29] that inflammation had spread from a joint, and affected the nerves as well as the muscles, giving rise to an ascending neuritis. If neuritis has occurred the muscle fibres will be found to be narrowed, and the connective tissue to have undergone proliferation. Vallat [30] noticed such a change in the muscle fibres, but he found that the

motor nerves were normal. These changes were all microscopical.

We are now face to face with a dilemma. We must either admit that the disease is one depending entirely on an abnormal nerve condition, or else we must formulate a new theory as to its causation. The nerve theory is quite unsatisfactory and unsatisfying. Could we account for the joint changes in some other way the nerve theory explains many of the symptoms, more especially the skin changes, and the muscular atrophy; but it does not explain the joint conditions. Owing to our want of knowledge as to the morbid processes which govern the vaso-motor and trophic impulses, we are unable to closely criticise any theory advanced with regard to their method and mode of action, especially in cases where only some abnormal disturbance of their functional activity exists, but so far no evidence has been produced which would give countenance to this theory. Without the joint lesions we should have no rheumatoid arthritis, and therefore unless a theory can explain this fact we have no right to consider it perfect. It has been mentioned already that many observers hold the changes to be similar to those which occur in tabes. To me they appear not to be so—they differ in appearance, in minute anatomy, and also in clinical history. In tabes the joint changes are due to a descending degeneration of the nerves, a change always found when looked for, and therefore their origin differs essentially from anything found in rheumatoid disease. To my mind this fact invalidates the whole argument. How, then, do we account for the disease? The theory which I advance and believe in is, that the disorder is due to a micro-organism which has as habitat the joints, and which there gives rise to soluble products which, when absorbed, pass to the central nervous system, giving rise to the nerve symptoms so common in this disease.

The arguments I would advance in favour of this view, apart from the actual bacteriological evidence, are shortly as follows:—

(1,) The frequent occurrence of this disease as a sequel to other forms of known infective disease. About 55 per cent. of my cases in which a definite cause is assigned, arise, I find, as the sequel of some infective antecedent disease, such as rheumatism, gonorrhœa, influenza, tonsillitis, typhoid fever, etc. In another 25 per cent. we find a history of disease of the female organs of generation, in 20 per cent. catarrhs of the gastro-intestinal and respiratory mucous membranes, chills and getting wet, and in 5 per cent. a history of direct injury. Stewart found 50 per cent. of his cases had suffered from previous infective diseases such as gonorrhœa, otitis media, subcutaneous abscesses, etc. Now while some of the above disorders obviously can act only as predisposing the soil to inroads of bacteria, others would supply the actual lesion through which the bacteria could gain access to the circulation. In this class would be tonsillitis, gastro-intestinal, respiratory and genito-urinary catarrhs, etc. A catarrh of the mucous membranes acts by producing mucous abrasions upon which organisms can settle; by weakening the epithelial cells in favour of the parasite; and by weakening the nutrition and vital energy of the body generally. With such conditions it is easy to see there will be little difficulty in gaining access to the circulation, and once having obtained a footing they will pass readily to all the tissues of the body.

(2,) Its numerous nerve symptoms for which no adequate nerve lesion has been found. This in my mind is one of the strongest arguments. Were the disease due to nerve troubles there can be no doubt adequate lesions would exist in the central nervous system. But there

is no evidence of their existence, and sufficient search has been made to render their existence impossible of remaining undiscovered. Yet, as the nerve symptoms do exist, we can only conclude that they are due to toxic action, and the probability is that the toxic products are produced by bacteria in the body and are not due to auto-formation.

(3,) The occurrence during the course of the disease of such disorders as pneumonia, pleurisy, pericarditis, endocarditis, etc., must necessarily imply an infective process. I find that about 3 per cent. of my cases developed either pneumonia or pleurisy during the time they were under my care, and about 17 per cent. developed endocardial or pericardial conditions after the onset of the disease.

(4,) Its polyarticular character, as Professor Bäumler says, is sufficient to suggest its infective nature.

(5,) Its course and nature also point this way. A disease marked by distinct and persistent swellings, showing periodic exacerbations, has all the characters of an infective trouble.

(6,) The presence of enlarged glands proximal to the affected joints must surely be caused by an infective materies morbi.

(7,) The result of treatment by guaiacol, salophen, etc., also surely points to a disease whose symptoms are mainly caused by bacterial products, for is not the principal action of these drugs to free the system of the albuminous products elaborated by micro-organisms by way of the kidneys ?

This theory is the one which has recently been largely accepted both at the Congress for Internal Medicine at Berlin, and at the British Medical Association Meeting at Montreal. Professor Bäumler says the possibility that a joint disease can be produced by lesions of

the mucous membranes of the genito-urinary apparatus, especially in females, or of the respiratory or gastro-intestinal tracts, suggests the probability of its infective character, and also explains its frequency in women who suffer from such disorders, as well as explains its appearance at, or about, the period of child-birth, or of the climacteric. It would also explain better what influence injury to the central nerve system has on its occurrence. He says the mere fact of its polyarticular character is enough to lead one to suppose we are dealing with an infective disease, the materies morbi of which circulating in the blood is carried to the synovial sacs, and to which they would appear to be specially susceptible. It is for this reason Waldman [80] desired to class the disease as an infective form of rheumatism, and which leads various French observers to describe it as "infecteux." Riva,[31] of Parma, in a recent paper, suggests the infective nature of the disease, and Prof. Stewart [19] and others at the British Medical Meeting at Montreal also adopt this view. Dr. Shingleton Smith [32] there stated that he considered it likely to be due to some infective agent, that it bore no relation to either tubercle or syphilis, but that its close pathological association with post-gonorrhœal arthritis renders it likely that some such parasitic organism as that described by Bannatyne, Wohlmann and Blaxall, was the infective agent of the disease, and that all the other numerous etiological factors commonly described might be swept away. He pointed out the differences between the early and the late stages of the disease and thought it probable that the parasitic stage was of limited duration, and that the later phenomena were all the sequelæ of the arthritis, in which perhaps mixed and secondary infections might play a part. On the other hand, Chvostek [33] at the Berlin discussion said there was

no ground for supposing that chronic rheumatism (the discussion was on Rheumatoid Arthritis,' which the Germans call one of the forms of chronic rheumatism) was a disease of bacterial origin. He said the great variety in the course of the disease was opposed to any such view; the only two characteristic features of the disease being the joint swellings and the transitory nature of these. He said the most satisfactory view of the disease was to regard it as due to toxins, produced in the body but not by micro-organisms. He also stated that a bacterial invasion gave rise to a very different kind of joint inflammation, characterized by its long duration, and the large amount of swelling which accompanied it. It seems to me he cannot have been talking of rheumatoid disease, for what joint disease has less transitory or more marked swellings? His arguments tell strongly in favour of a bacterial origin. So far, therefore, the balance of opinion is in favour of my view. Buzzard points out that frequent and more or less prolonged periods of remission of symptoms, and the occurrence from time to time of fresh outbursts in a disease, point mainly to an infective origin, and remind one clearly of what occurs in syphilis, a typically infective disease.[16] Assuming this theory is accepted, we know that the chief lesions must be due, not to the mechanical presence of the micro-organisms themselves, but to their metabolic products. We have therefore an infection followed by an intoxication.

The infection consists in the micro-organisms selecting a suitable nidus in which they may grow and propagate, and, like all other pathogenic bacteria, they exhibit a selective power in their choice of a habitat, which never varies. In the joints, Dr. Wohlmann and I found positive proof that the micro-organisms grow and propagate, for their presence can be demonstrated in

the joint fluids by staining, and in the tissues on section. What governs this selective power we know not; but it appears curious, that out of all the sites to which they obtain access, they should, as far as we at present know, only choose the joints. We know, that in relation to different causes of disease, the various tissues of the body exercise the most markedly different influences, even though the cells constituting these various tissues have originally sprung from the same cell. This difference is not limited to the various tissues of the same species of animal, for, when we compare different species, we find that even the same organ or form of tissue may present the most marked differences in relation to the factors giving rise to disease. For example, we see how in man the liver is an inhospitable host to the bacillus of tubercle. But it is not so with the liver of the ox or the guinea-pig. Of similar import is the fact, that if we examine every one of the pathogenic microbes, we will find different species of animals presenting very varying degrees of susceptibility. Even in the case of such a disorder as anthrax, there are all varieties amongst the various species, from immunity in the frog, to extreme susceptibility, as in the mouse and guinea-pig. This variation in susceptibility applies not only to species, but to varieties and races of animals and men. It is well known that the white rat presents an almost complete immunity to anthrax, and that the Algerian sheep are much less susceptible than other breeds. A similar fact is observed in man in this respect, that negroes are, as compared with white men, singularly insusceptible to yellow fever. Again it may be noted that joints are specially liable to bacterial infection, *e.g.*, such diseases as pyæmia and gonorrhœa, and if, as seems likely, acute rheumatism is due to bacteria, or their products, we have yet further proof of this peculiar liability.

In rheumatoid arthritis, as in acute rheumatism, ulcerative endocarditis, etc., it is possible that the bacteria grow also on the endocardium and pericardium, as otherwise it is difficult to account for certain of the symptoms. It is probable that they grow freely in the lesions through which they gain entrance, and possibly also in other localities. But having no proof one way or another on this point, we must leave it for future consideration. On the other hand, in the joints themselves we have positive proof that the organisms grow and propagate freely, doing so not only in the synovial fluid and membrane, but also in the ligamentous, cartilaginous, and, to a less extent, in the bony structures. Their presence gives rise to acute inflammatory changes leading to ulceration, erosion, and destruction of the hard as well as of the soft tissues. This process varies in intensity and, usually as the disease progresses, is accompanied by a coincident, but varying amount of reparative change which may end in a general hardening and thickening of bones, cartilage and ligaments. This change appears to occur either when the bacteria have exhausted the pabulum on which they exist or else it is an attempt on the part of nature to limit and shut off the disease. Possibly the production of toxic products may play some part in the matter. The joint symptoms, which are due to the local action of the micro-organisms and their products, may therefore be regarded as **primary** or **essential**; whilst those which are due to their indirect action, by the absorption of their products, may be regarded as **secondary** or **symptomatic.** Although these latter vary in every case, not only in intensity and in nature, yet they would appear to have a common toxæmic origin; and some symptom of this toxæmia is invariably present.

The effects of the intoxication are principally seen by

their action on the nervous system, and to explain this picking out of certain areas, besides the toxic theory we must add a supplementary hypothesis of "susceptibility of parts." Edinger[34] accounts for this susceptibility on the theory that those parts first degenerate which suffer the heaviest demands upon their function. With regard to the severity of the toxic effects, Van Geisen[35] says that the nerve degeneration is in direct ratio to the duration of the action of the poison. Changes produced by acute poisoning may be recovered from, although the degeneration may be profound, but prolonged toxic action destroys the cell, and the integrity is irremediable. The whole course, duration, and termination of toxic disease depends upon the course of parenchymatous degeneration, controlled by the duration and intensity factors of the poison.

How then do we apply these facts to what we find in rheumatoid arthritis? Let us first take the case of the **muscular atrophy** which is one of the most constant symptoms of the disease. Apart from true rheumatoid atrophy, we must remember that atrophy may occur as a consequence of a secondary neuritis. Such a condition has been described by Sabourin,[36] Vallat,[30] Strümpell,[28] Duplay and Cazin,[13] and is of less interest than the true rheumatoidal atrophy, and can be easily distinguished, as it presents all the characters of ordinary muscular atrophy in the re-action of degeneration and alteration in the muscle structure, etc. This is absent in the true form, in which the extensors are principally, but not exclusively affected. The selective character of the atrophy is sufficient proof that the changes cannot be set down to mere disuse. The atrophy therefore, is in all probability, due to an abnormal condition of the multipolar nerve cells in the anterior cornua depending

on toxic poisoning.* For it is reasonable to suppose that, given a soluble poison circulating in the blood, some areas in the central nerve system should be affected, and these all the more, especially as they may be predisposed to it by reflex irritation from the joints. The areas to be affected will be those which have the heaviest demands on their function. That such a reflex irritation does occur has been stated by many observers, and has been even said to be sufficient to cause the atrophy itself (Paget, Vulpian,[24] Charcot, and others). It has been argued that, assuming a derangement of the motor cells of the cord determined by the morbid impulses from the joint nerves, the influences from the motor cells will determine the alterations in the muscle nutrition. In the light of the discovery of the micro-organisms, and of recent observations with regard to the action of toxins on the nerve system, we may disregard this reflex irritation except in so far as only to regard it as a predisposing cause. On turning again to the cells themselves, we find, according to Ferrier,[38] that the cell body with its nucleus is primarily concerned in the nutrition of the motor nerve, and its correlated muscular fibre, while the dendritic processes serve to convey incitations to functional activity. He also states that lesions of these processes may cause paralysis with all the symptoms of a spinal paralysis, but with no muscular degeneration. If such a condition can exist, might we not consider it possible that by the action of a toxic body,

* The path of motor innervation is composed of two portions, *(a)* the pyramidal cell with its dendritic processes, and centrifugal or axis cylinder process which courses along the pyramidal tract, and *(b)* the spinal multipolar cell with its processes, and axis cylinder process ending in the muscle fibre. It has been shown by Golgi's [37] method of staining that the pyramidal axis cylinder ends in an arborescence which merely comes into contact with the spinal cell or interlaces with its dendritic processes, and there is no actual continuity.

the cell's action might by itself be so lowered or held in abeyance that nutritional changes in the muscles would ensue without much disturbance of the conductive faculty of the processes, and also without any degeneration of the muscle beyond wasting? Any disease attacking the central nervous system and causing actual change, never attacks the cells alone, or the fibres alone; for the neuron (the compound of cell, axis cylinder, and terminal branching) is one coherent entity. So the lesion in this case must consist of a depression of the function of certain cells, for if we compare the clinical characters of the atrophy with that of progressive muscular atrophy we will see that no actual lesion can exist. In progressive muscular atrophy, of which Buzzard [16] says some mode of infection would best explain the clinical features and the pathological anatomy, we have a slowly progressive lesion of the ganglion cells and their prolongation in the axis cylinders of the nerve fibres. In this disease, where the atrophy is marked by the reaction of degeneration, there are actual degeneration changes in the cord, whilst in rheumatoid arthritis, with no reaction of degeneration, there are no changes in the cord. No theory will account for this unless it be as I have said. The cell's vitality must be lowered. In one class of cases, of which those mentioned by Dr. Spender [39] may be taken as typical examples, we must assume that the action on the cells has been so great as actually to give rise to a distinct lesion, and this spreading upwards in the pyramidal tract has finally come to affect the bulbar neuclei. Folli's [10] discovery of atrophy of the motor cells, goes a long way to confirm this theory. What was probably only at first a depression of function due to the changes set up by the rheumatoid toxin had apparently, in the long run, become actual organic change. Miller,[40] speaking of the muscular

wasting seen in phthisis, says it is due to a vaso-contraction affecting certain centres of the cord; the vaso-contraction being caused by the products of the bacilli, just as the products of pyogenic organisms cause vaso-dilatation and diapedesis.

With regard to the selective site of the muscular atrophy, and apart from Edinger's theory (see p. 32), we find Dr. Ferrier[38] saying, "It is not unreasonable to suppose that the degree of representation, and therefore the trophic strength, of the extensors in the anterior cornua is less than that of the flexors, while such extensors as have the most numerous connections with the spinal segments would have a greater vital resistance than those whose segments are fewest." From this we may deduct that those muscles with the lowest trophic representation will be those which are first, and most affected, in any disease which lowers the vitality of the nerves and nerve centres. Duplay and Cazin[13] have suggested that it is due to the anatomical relationship between the nerves which supply the joint corpuscles, and those which supply the affected muscles. This does not explain it all, however, and Dr. Ferrier's explanation seems the more probable, and the more easily understood, especially if we add that reflex impulses may possibly help in the selection.

It has been proved that certain toxins have the power of producing changes in the vaso-motor system, and also in the trophic condition of the skin. It is thus that we account for the **local sweatings** and **pigmentation.** We know that normal pigment is formed from a particular product of metabolism of the cutis, being formed both in the ordinary epithelial cells and in the connective tissue cells. These connective tissue pigment cells are the regulators of the metabolic process, as they consume the surplus pigment-forming substance. The abnormal pig-

mentation of rheumatoid arthritis is probably due to a local increase in the formation of the normal pigment, consequent upon some abnormal innervation, and to a deficient consumption of the surplus by the connective tissue cells. The **vaso-motor changes** are in all probability due to the centre situated in the intermedio-lateral tract, being affected in a similar fashion to those in the anterior cornua.

One of the greatest points of interest is the **tachycardia**. Bezançon [41] states that tachycardia may in some cases be due to pressure on the vagus, but he suggests that more often it is due to the absorption of certain toxins. He cites the case of the bacillus tuberculosis, and also of certain staphylococci, streptococci, etc., of the secondary purulent infection so common in phthisis. Bouchard obtained from tuberculin a substance to which he gave the name ectasine, which had the property of producing dilatation of the vessels. Toxins, with similar powers, have been obtained from the product of the bacillus pyocyaneus by Charrin and Gley; and from those of the staphylococcus aureus by Arloing. By acting as vaso-dilators these substances would tend to produce tachycardia, since the heart tends to act more rapidly as the peripheral friction diminishes. In other cases the toxins, by giving rise to a neuritis of the vagus may cause it. Vierordt in a case of phthisis found such a neuritis, as evidenced by a great number of vagus fibres having undergone degeneration and atrophy. With regard to the local sweating, it is probably due to paresis, caused by the toxin acting on the sudoriferous, and vaso-motor centre of the bulb. Similar action is seen in influenza (Semmola[42]).

Anæmia in many cases is marked. Now it has been found by Hunter [43] that, in all probability, pernicious anæmia is caused by the presence of bacterial poisons, just as it has been found to occur from the

presence of cadaveric poisons, and analogous ferments. Such being the case it requires little imagination to conceive that a similar process may occur in rheumatoid arthritis. These bacterial poisons would seem to act by a hæmolytic process which is specially limited in its action to the portal blood. There are some special points of interest in the anæmia of rheumatoid arthritis. These are the diminution of the hæmoglobin value of the red cells and the increase in the number of the white. Forsbrooke also notes this diminution of the hæmoglobin. According to Oster we have three classes of anæmia :—

(1,) Those in which the percentage of hæmoglobin in each corpuscle remains the same, and the percentage of colouring matter corresponds to the percentage of the corpuscles. This is usually seen in anæmia due to hæmorrhage, or arising from some organic disease. It may be noted that Laker [44] and Mackenzie [45] both point out that in malignant disease the hæmoglobin value is decreased. The former states that from this fact alone one can diagnose the nature of the tumour, at least in so far as to say it is malignant or benign.

(2,) Those in which the hæmoglobin is reduced out of all proportion to the reduction of the corpuscles, so that the individual value of each red cell in colouring matter may be greatly lowered. Chlorosis is the typical example of this class.

(3,) Those in which the percentage of hæmoglobin is increased, and in which, therefore, the anæmia is not so great as the reduction would appear to indicate. This is seen most markedly in pernicious anæmia.

In rheumatoid arthritis, then, we have to do with an anæmia belonging to the second class—in fact an oligochromæmia.

We have now to ask ourselves why, in one form of anæmia, the hæmoglobin value should be lessened, and

in another increased? Where it remains constant it is probably due to a loss of blood as a whole, whereas, in the other cases, it must be due to some abnormal condition having a direct influence on the blood cells or their contents. We know that anæmia implies a want in the adjustment between the gains and the losses of the blood—defective hæmogenesis or excessive hæmolysis, the former depending upon deficiencies in quantity or quality of the food, insanitary surroundings or mode of life, inherited or acquired defect in the hæmopoietic viscera etc., and the latter on the processes of fever and inflammation, or to the presence of deleterious substances in the blood. With the former condition we have nothing to do. It would appear as if most forms of anæmia in which destruction of the red cells and their contents is the typical feature, must depend, for their occurrence, on some substance, harmful to their existence, circulating throughout the system. Dr. Hunter [46] says that blood destruction is of two kinds — *(a)* **passive,** which is the ultimate destiny of the red corpuscles, and which being a process of natural decay is evidenced by the presence of pigment in the spleen, liver and bone-marrow; and *(b)* **active,** in which the hæmoglobin escapes from the corpuscles into the plasma, and is in great part excreted by the liver as bile pigment. In health no trace of this breaking up and excretion of free hæmoglobin is found, but in such a disease as pernicious anæmia there is abundant evidence of it in the liver cells. This has been found not only in pernicious anæmia but also in malaria, and as the result of certain poisons which destroy the blood. Now, this destruction of the blood would not appear to take place so much in the liver as one would expect, as in the spleen and to a less extent in the gastro-intestinal capillaries. This Hunter has demonstrated by many beautiful experiments. He found that

almost all hæmolytic process was stopped by removal of the spleen, whilst experimenting with toluylenediamin. The chief function of the liver would, therefore, appear to be the disposal of the products of hæmolysis. He goes on further to show that certain substances, such as toluylenediamin, act on the blood indirectly and depend for their effect on the action of certain cells and especially of those of the spleen; whereas such substances as pyrogallic acid, glycerine, distilled water, etc., act directly, and depend on the quantity injected for their effect.

This, however, does not help us much in solving the question as to why, in one case, the same class of poison should produce an increase in the hæmoglobin value, whilst in another it diminishes it. Are we to suppose that each individual poison possesses a selective action, and that it has the power of picking out one constituent only, of the blood, for special attention? This is possible from what we know of the action of bacterial poisons, but it is hardly probable. It appears to me more likely that the different classes of bacterial poisons will have different effects—thus the toxic albumens may have the power of dissolving out the hæmoglobin without destroying the cell (see the action of snake poison and that of malaria) and the ptomaines may be more destructive to the life of a corpuscle than to its contents.

In rheumatism we have an acute disease which is most probably due to an infective organism (Newsholme),[47] and in which Dr. Garrod [48] finds a loss of the red corpuscles with a corresponding loss of hæmoglobin—the corpuscular value remaining constant. In some cases, during the course of the disease, there is, however, a tendency to a decrease in the corpuscle value of a transitory nature, but which may become more permanent during convalescence, producing a more or less chronic anæmia. In malaria, a disease due to an infective

protozoa in all respects resembling a bacterial infection,[49] we have, according to many observers (see Mannaberg,[50] Evans,[51] etc.), a reduction in the hæmoglobin value, especially after the paroxysms. Mannaberg says that "for several days after the last paroxysm of fever the proportion of hæmoglobin still fell." He gives as explanation of this the supposition that the hæmoglobin is dissolved out by the parasitic poison circulating in the liquor sanguinis. Evans[51] notes a reduction in the number of the red corpuscles, and also of the hæmoglobin—the loss of the latter exceeding that of the former. He found no change in the number of the white corpuscles. Finally, in pernicious anæmia, Dr. Hunter maintains that the anæmia is due to the presence of bacterial poisons acting on the blood in the portal capillaries, thus causing an anæmia in which there is an increase in the hæmoglobin value of the individual cells.

I take it that in the first disease, as there is no increase in the number of the white corpuscles, we are dealing with a pure toxæmia—the bacteria themselves not entering into the blood. And in the second we have a mixed cause—the parasite not only destroying the cells and their contents by their presence, but their toxins, by dissolving out the hæmoglobin, produce a diminished hæmoglobin value. And in the last case we are probably dealing with an alkaloidal poison absorbed from the intestinal canal. According to Cohnheim[52] certain substances, of which snake poison is one, has the effect of dissolving the blood corpuscles, and Maragliano[53] states that there are certain pathological conditions in which the blood serum exercises a destructive influence upon the red cells, which causes them to give up their hæmoglobin to the menstruum, and that it then disappears from the blood. In the present state of our knowledge one does not like to dogmatise, but it would appear to

me as if the two classes of bacterial poisons (ptomaines and albumoses) had each distinctive actions. In rheumatoid arthritis we are dealing with a disease in which the micro-organisms exist in the blood, but they, as far as I know, do not seem to destroy it as do the malarial parasites, and that probably, therefore, the anæmia is to a great extent due to the action of their toxic products, dissolved and circulating in the blood.

The increase in the number of white corpuscles is of interest as it is found in most infective conditions, and according to Hunter [54] the increase is roughly proportional to the severity of the disease. Habershon [55] says he has noticed an increase, not only after the introduction of alkaline carbonates, but also from the presence of toxins in the blood. Should bacteria themselves be present, the destruction of the red cells will probably be greater and occur sooner than where their products only exist.

Part II.

Assuming that the disease is of an infectious nature, we find the predisposing causes are all those which, by some means or other, lower the constitutional state. The tissues, in health, being able to resist the inroads of disease it is only among such influences as would bring the body generally into a condition of lowered vitality, that we look for predisposing causes. Of these causes the principal are :—

1. **Heredity.**—It is difficult to prove direct inheritance, not only on account of the difficulty in the diagnosis, but also on account of the confusion which exists as to what form of disease the term rheumatoid arthritis should be strictly applied to. It may happen likewise, even although the proper nomenclature is understood in the

individual cases, that the disease may have passed over one or more generations. It may be described as occurring sporadically; and that, out of a family of brothers and sisters, some are affected, but others escape. Heredity, therefore, is very hard to trace. It is known besides that an inherited tendency to disease does not in all cases manifest itself in an exact reproduction of the morbid peculiarity of the parent in the child, but may tend to give rise to allied conditions. Thus, it may happen, that in those inheriting an arthritic diathesis, in some rheumatoid arthritis may develop, in others gout, and in others rheumatism. Statistics go to prove that a certain diathetic predisposition to arthritic disease does exist. By this we mean a diathesis in general, not in special, and in all cases it is easier to trace and to prove this inheritance of a diathesis than of a disease itself. One member of a family may have gout, one rheumatism, whilst yet another rheumatoid arthritis. In the case of gout and rheumatism heredity has been clearly proved, and this is probably due to the fact that they are both diseases well known and have been readily recognised for ages, whereas rheumatoid arthritis has not. By some it has been said also, to be peculiarly liable to occur in those inheriting a tendency to phthisis. This is as one would expect, but there is nothing in common between the two diseases, except that a tuberculous tendency may, by lowering the resistance, tend to bring about rheumatoid changes, and it is only in this connection that there can be any association between the two disorders. The rheumatoid materies morbi would, in such cases, find a system weakened and unprepared to resist its inroads, and would therefore in all probability fall an easy prey.

As a cause, heredity was recognised early in the history of the complaint, for we find that Heberden,[56]

Adams[57] and Fuller,[58] amongst the early observers, all mention it. Coming down to more recent times we find a history of heredity was obtained in 11 out of 41 cases by Charcot,[59] and in 10 out of 45 by Trastour.[60] These statistics are quite unreliable, however, as these observers only regarded rheumatoid arthritis as one of the many forms of rheumatism, and as such the family history was taken. Garrod[61] traced in 84 out of 500 a direct descent, giving a percentage of 16·8. The average percentage of heredity, in rheumatism (taking the results of Fuller, Syers, Pye-Smith, Garrod, etc.), is 23·9. When we consider the inheritance of other forms of arthritic disease, in rheumatoid arthritis the percentage is much greater. Garrod[62] gives a percentage of 43·2. On further analysis he mentions that there was a history of gout in 20 per cent., whilst only 12·8 gave one of rheumatism. This is very remarkable, and I have quite failed to verify it. Sir A. Garrod and Sir Dyce Duckworth point out that the disease is most common in female members of gouty families. My statistics do not bear this out, for taking three years at the Bath Royal Mineral Water Hospital (1894-1897), I had 293 patients suffering from rheumatoid arthritis, and of these only 15 gave a history of direct inheritance. In only a very few could gout be clearly traced. In several there was a history of rheumatism affecting a brother or sister, and in 36 affecting a father or mother. Heredity does not seem to render a patient more liable to be attacked in early life, but it does seem to affect the acuteness of the disorder.

2. Sex.—There can be no doubt that the disease is much more common in women than in men. Out of 293 cases 41 were in men, and the rest in women (13·9 and 86·1 per cent.). Gout affects men more commonly, whereas rheumatism does so in nearly equal propor-

tions. Haygarth [63] found 1 man to 34 affected, and Garrod [64] found that it occurred in 411 females to 89 males (82·2 and 17·8 per cent.). As was pointed out by Adams, Senator, and others, the joints most affected in men, are the larger ones, such as the hip or shoulder, and in women, the smaller ones. Charcot, Trousseau,[65] Duckworth, and others, have also observed it to be more common in women. This frequency in women is almost certainly due to the frequency of some genito-urinary derangement, some abnormal condition of which readily enables the micro-organisms to obtain access to the blood, and thence to the joints. In the case of children rheumatoid arthritis is more common in boys than in girls—the younger the child the greater the proportion of males. As puberty is approached this diminishes until the proportion of females equals, and finally greatly exceeds that of males.

3. Age.—Much has been written about the age at which the disease most commonly commences. By most it is held to be essentially a disease of the early, degenerative period. According to my experience many of the acutest cases occur, however, in young adults, and often even in children. Dr. A. E. Garrod[67] shows that the commencement of the disease in females steadily increases with each five-yearly period, until the one from 45 to 50 is reached, after which the numbers rapidly fall. In males, on the other hand, the decrease does not occur until 70 has been reached and in them also there is no steady increase, but two maxima exist, one between 30 and 35, and the other between 50 and 55. The special liability of women between the ages of 40 and 50, is probably due to the occurrence of the climacteric. In women there are two great periods of life—the period of puberty, and that of the climacteric. The former is a time of great strain, both

mentally and physically, not only on account of the new conditions which the reproductive organs have taken on, but also on account of the general bodily conditions induced thereby. It is a period attended by a general aptitude for disease, as there seems to be a special connection between the physiological processes going on, and the general bodily health. At the same time women seem liable to attacks of disease for which no reason can be assigned. The period of the climacteric is at the other end of life, answering in many respects to the period of puberty in being a time in which the whole system is in a state of unrest, unstable and ready to develop unhealthy tendencies. Unfortunately it is a degenerative process, and, from its very nature, we would expect to find it the more productive of mischief. The sudden fall in the number of cases occurring after the menopause is probably due to the fact that, all uterine activity having ceased, there are fewer roads by which micro-organisms can gain access to the system. It is almost certain that a climacteric occurs in men in a similar fashion, but it is not so marked, and probably occurs later in life. The following is an analysis of 293 cases :—

AGES OF FIRST OCCURRENCE.	FEMALES.	MALES.
Between 10 and 20	14	5
,, 20 ,, 30	54	5
,, 30 ,, 40	78	8
,, 40 ,, 50	50	11
,, 50 ,, 60	45	9
,, 60 ,, over	11	3
Totals	252	41

4. **Catarrh of the Mucous Membranes.**—How far a

catarrh of the mucous membranes of the respiratory, gastro-intestinal, or genito-urinary systems acts as a predisposing cause, it is hard to say; but that it is through its agency that the micro-organisms finally gain a footing is almost undoubted. I have traced the onset of the disease in several cases, almost with absolute certainty, to chronic catarrhal tonsillitis; several to the onset of dyspeptic conditions, and a still larger number to the onset of genito-urinary troubles. It is a frequent sequela of confinements, and, more rarely, begins during pregnancy. Uterine derangements are responsible for the onset of many disorders, but none more markedly so than rheumatoid disease; and how can we wonder at it, when we find, as a consequence of some local irregularity, women in a state of worry and anxiety, sleepless with much pain and nerve exhaustion, their mental and physical powers being both at their lowest ebb? Dr. Ord laid special stress upon this fact, and I think it is well merited, though my reasons are different. He noticed that, in certain instances, the disease in the joints was limited to one side; and in these cases there was ovarian pain, and tenderness on the same side as the joint lesions. He also noticed paroxysms of pain occurred with the monthly periods. He considered these uterine and ovarian derangements to be the cause of the disease, through reflex action. To my mind, it is more probable that the ovarian and uterine derangements act only by affording a lesion through which the micro-organisms may reach the circulation; and, by the induced irritation and debility, render the system so lowered and impaired as readily to fall a victim.

In 293 cases, 18 occurred after confinements; 2 during pregnancy; 2 after a miscarriage; and one after marriage.

In a large number there was irregularity in the monthly functions, but I rarely could trace a case directly to these disorders. Garrod says that 105 out of 176 were normal in their menstruation. Five occurred soon after a confinement, 3 after miscarriages, and 3 during pregnancy.

5. Emotional Causes.—The influence of these is not confined to the period immediately preceding the onset of the disease, but they also to a certain extent influence the progress of the disorder. Over and over again do we find patients say they are worse after any anxiety or worry, and it has been known even to arise after a period of prolonged worry; but in such cases worry probably only acts by lowering the tone of the constitution. Stewart[19] mentions 4 cases as having been caused by worry. Other mental causes assigned are sudden shock and fright. Both Kohts[68] and Leyden[69] mention cases in which severe shock was the cause—the shock arising from shells bursting in time of war.

6. Atmospheric Conditions.—Rheumatoid arthritis is most commonly met with under those influences most favourable to the prevalence of catarrhal and inflammatory affections of the air and digestive tracts, that is, on cold and damp soils with a variable temperature, and, as we know, at those seasons of the year—the spring and autumn—when these conditions are most likely to prevail. Professor Charcot regarded a combination of damp and cold as the most potent cause. He was of the opinion that exposure to such influences must be prolonged, and that articular lesions did not necessarily arise until some time had elapsed. Many sufferers corroborate this and ascribe the onset of their complaint to dampness, and there is no doubt that cold and damp often markedly increase the misery of the wretched patients. The disease is more common in Ireland than in

England, and this is accounted for by the prevalence of damp in the former country, and Adams [70] has pointed out that it is specially common in Holland. Stewart points out that it is very rare in Canada. This one would expect in a country with such a dry air. Although a dry climate is least favourable to its development, it is not unknown in any locality. In this respect we are apt to confound, and it is difficult to avoid confounding, its indirect effects as predisposing agents with its direct effects as exciting cause. Further, when we would test the relative influences of atmospheric conditions, our endeavours to arrive at a just conclusion are seriously hampered by the co-existence with them (but partly no doubt arising out of them) of peculiarities of habit, and modes of life, and other special conditions of unhealthiness. Out of 293 cases, 26 developed after getting wet, or after a chill.

7. **Injury.**—Injury, as traumatism pure and simple, has not a marked effect on the occurrence of acute rheumatoid arthritis. Only a few cases have I been able to trace to this, but if we look at the term in its wider sense it comes to have a much more important bearing. A direct injury, in its immediate consequences, may appear so trifling as to merit little or no attention, yet it may, in its ultimate consequences, end in the crippling and loss of the use of an important member of the body. Orth and Wysokowitsch [71] have shown that traumatic lesions will cause a local predisposition to infective processes. Occasionally, but more rarely, it appears to follow on some injury which has set up some acute inflammatory condition. In one case I found it occur subsequent to fracture of a patella, and whilst the patient was in the recumbent position in consequence of this fracture. A history of such direct injury, and its consequences, is rare. One more often hears of injury

after the joints are diseased, and then the question of effect and cause comes to be a difficult one. Looking at it from a broader point of view our idea of the importance of injury, as a cause, alters. In 293 cases 46 occurred after acute or chronic rheumatism. I here regard the injury caused to a joint, when caused by rheumatism, gout, gonorrhœa, or any other form of arthritis which may so frequently precede a rheumatoid onset as having more or less the nature of a direct injury. That rheumatoid disease frequently follows attacks of such diseases is not to be wondered at, when we remember the injury they do to a joint, and when we consider that rheumatism, and most other forms of acute arthritis, are probably caused by micro-organisms or their products—at least, at present there seems to be good ground for believing that such is the case ([72] and [73]). Just as one form of micro-organism or its poison can inhibit the growth of another so does the converse occur. Roger[74] has shown that rabbits which are naturally immune will succumb to quarter-evil if simultaneously the chemical products of the bacillus prodigiosus, proteus vulgaris, or staphylococcus be injected. Other vegetable bodies, such as the vegetable ferments, have the same effect. Klein[75] and others have shown that the simultaneous injection of the bacillus prodigiosus and various pyogenic germs with the bacillus of tetanus will render animals capable of resisting a simple infection of the tetanus bacillus extremely susceptible. Again, the virulence of the bacillus diphtheriæ may be greatly increased by the inoculation of the bacillus pyocyaneus. But we must remember that while certain diseases render the tissues more susceptible to the attacks of other diseases, yet certain micro-organisms lose their virulence when confined in closed cavities such as a joint, possibly from the action of their own products.[76] What the effect of

rheumatism and its allied disorders is we do not know, and it is a moot point, whether they act by reducing the resistant power which normally exists in all tissues, but in this case more especially in the joints, or else of the blood. But we do know, as has been stated by Ewing [77] and Fodor,[78] that anything which reduces the blood's alkalinity reduces its germicidal power. Ewing found that normal blood serum is a powerful protective agent against the inroads of bacterial infection, and that toxins act harmfully, not merely by their direct effect, but also because they lower the resistant power of the blood against secondary infections. He found that snake poison, which in its nature belongs to the same class of poisons as those formed by bacteria, greatly lessens the blood's germicidal power. Fodor records a number of experiments showing the influence of the alkalinity of the blood on diseases produced by micro-organisms. Four series of experiments on animals are first reported which show clearly that, by the administration of alkalies (sodium bicarbonate by the mouth or by subcutaneous injection), the power of resistance against infection with cultures of anthrax bacilli is greatly increased. The normal alkalinity of the blood was determined by the examination of seventy-six healthy rabbits, and four experiments are reported showing the increase in the alkalinity of the blood which occurs after the administration of sodium bicarbonate. He then records the results of a large number of observations on the alkalinity of the blood in rabbits after infection with the bacilli of anthrax, cholera, typhoid fever, tuberculosis, and erysipelas. These observations show that in the living organism, after infection with certain bacilli, there is first an increase of the alkalinity of the blood and then a diminution of the same, more or less. If the infection is fatal, the

diminution of the alkalinity is marked and progressive; if not fatal, the diminution is slight, and is followed by an increase of the same, in consequence of which the alkalinity of the blood becomes permanently higher than before the infection. Thus there exists a connection between the pathological action of certain bacteria and the alkalinity of the blood. Those rabbits which have the greater alkalinity of the blood, as well as those in which the alkalinity of the blood is increased to a greater extent after infection, have greater power of resistance against certain infectious organisms (anthrax bacilli) than the rabbits in which the alkalinity of the blood is less. It appears, therefore, that the degree of alkalinity of the blood, as well as the power of the organism to increase this alkalinity with corresponding intensity after infection, is of essential influence upon immunity.

Although we are still in the dark as to their mode of action there is no doubt as to the frequency with which rheumatoid arthritis follows on infective processes affecting one or more joints. Stewart [19] says 50 per cent. of his cases had suffered from previous infective diseases, more especially gonorrhœa or gonorrhœal arthritis, and it is worthy of remark that although the gonorrhœal arthritis was confined to one joint yet the subsequent rheumatoid arthritis attack was poly-articular. He concludes that a mono-joint infection may predispose to a general joint affection. Chvostek [79] says that in considering joint invasions we must bear in mind as causative factors, not only toxins of those micro-organisms which we believe to be infective, but also those chemico-toxic substances produced by indirect bacterial activity.

Such then are the more common predisposing causes, and herewith I append a list of those assigned in 132 cases out of 293:—

After confinement	18
,, miscarriage	3
,, marriage	1
During pregnancy	2
After acute rheumatism*	41
,, chronic rheumatism	6
,, diphtheria	2
,, influenza	11
,, tonsillitis	7
,, typhoid fever	2
,, dyspepsia	2
,, injury	6
,, concussion of the spine	1
,, necrosis of the jaw from caries of teeth	1
,, hard work	4
,, getting wet or from a chill	25
	132

The other 161 cases gave histories too unreliable, or could give no cause.

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* With regard to acute rheumatism being assigned as a cause, some confusion must arise from a primary attack of rheumatoid arthritis being described as one of acute rheumatism. Many such cases are pure acute rheumatoidal attacks, and statistics on this point, therefore, are apt to be unreliable and misleading.

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CHAPTER III.

PATHOLOGICAL ANATOMY AND BACTERIOLOGY.

Degenerative Character of Changes—Point of Origin—How the Bacteria gain Access—Naked Eye Appearances—Changes in Synovial Membrane—Loose bodies—Ligaments—Characters of Synovia—Changes in the Cartilages—Cornil and Ranvier's Views—Erosion—Proliferation—Lipping—Changes in Bones—Rarefication — Osteo-sclerosis — Volkmann — Changes in the Muscles—Central Nerve Changes—Peripheral Nerves—Cardiac Changes — Kidney — Blood — Glands — Fibrous Nodules — Heberden's Nodes—Situation and mode of Growth—Gout as a Cause—Their Nature—Various Observers' Views—Bacteriology.

On examining after death the changes in rheumatoid arthritis, we are at once struck by the extensive and degenerative character of the lesions. Much has been written about these, but owing to the scarcity of *post-mortem* material, until the acute stages at least are past, few observers agree. Colles[1] and Todd[2] held that the disease was not inflammatory in nature, whilst Adams,[3] Brodie,[4] and Cruveilhier,[5] did; Fuller[6] looked upon it as a disorder of nutrition, rather than the result of inflammation; and Senator[7] regarded the changes as partly inflammatory, and partly degenerative, whilst Garrod[8] also held this view. Rindfleisch[9] stated that the disease was essentially one of those lingering inflammatory conditions which accompany the decay of the organism, like atheromatous disease of the internal coat of the arteries. He said that the inflammation, not being powerful enough to cause suppuration, sets up a

hyper-plastic overgrowth. Trousseau,[10] in his clinical lectures, says "the synovial membrane demonstrates its inflammatory origin." From what we know of the disease its changes must be inflammatory in origin, and they probably begin in the synovial membrane, and spread from thence to the cartilage and deeper structures. In acute rheumatoid arthritis the changes are, of course, principally destructive in character; but as the disease progresses and becomes more chronic, more and more reparative change occurs, leading to cartilaginous, osteophytic and ligamentous hardening and overgrowth. As I have said, in the acute cases the inflammatory and destructive element is in excess, whilst in the chronic or osteo-arthritic, the fibroid or sclerotic is.

Brodie, Adams, and others, thought that the disease commenced in the synovial membrane, whilst Volkmann, Billroth [11] and Garrod consider it starts in the cartilages. Given a micro-organism circulating in the blood, I think it probable that the synovial membrane will be the first to suffer, and after gaining access to the joint fluid, one would expect it to spread rapidly and affect almost simultaneously, by dissemination, the whole of the internal surface of the synovial cavity. The question is, How do the micro-organisms gain access to the joint cavity in the first instance? The probability is that they do so by setting up an endarteritis in one of the small vessels on the surface of the synovial membrane, with a diffuse cell exudation, and this, by extension and rupture, breaking into the joint cavity, liberates them for further mischief. As regards this point the experiments by Chvostek [12] are of interest as they show: (1,) That the walls of blood-vessels, not evidently altered anatomically, are permeable to bacteria; (2,) That the anatomical structure of the synovia and its vessels is an obstacle, and bacteria enter the joints considerably later than they

do the kidneys through the renal vessels; (3,) That the exit of bacteria depends on (*a*,) their kind—thus staphylococci pass most readily, then streptococci, and lastly the bacteria coli. This is probably due to the relative virulence of each micro-organism for each individual animal, and also to certain tissues being more susceptible to certain bacilli than others. (*b*,) Their virulence—in this connection the action of toxins must be considered; (*c*,) other factors, chiefly nervous—for instance, section of a nerve hastens the exit of bacteria. If this theory be correct it, of course, makes the synovial membrane far more likely to be primarily affected than the cartilages. However, I do not think one can lay much stress on which portion is primarily affected, nor is it of vital importance.

1. **General appearance of the joint.**—To the eye we find an affected joint presents the following general characteristics: It is swollen and increased in size, usually, in the acute stages, in a characteristic ovoid manner; but which, in the more chronic stages, becomes less marked and more irregular. In the chronic forms there is often deformity produced, partly by out-growth from the cartilages or bones, and partly by twisting or distortion of the joint; the deformity may be due to both or either of these causes. On opening the joint we probably find some fluid, certainly in the earlier, and acuter cases almost always. Trousseau remarks that the joint is often distended by hydrarthrosis. This presence of synovial fluid during life is often deceptive, and the doughy or pulpy synovial membrane produces a feeling difficult to differentiate from that of fluid. The synovial membrane we notice is thickened—in acute cases this thickening being soft and pulpy, whilst in the chronic stages it is hard and dense, the ligaments being affected in a similar way, and, in very chronic

cases, may present cartilaginous or even bony deposits. The inner surface of the synovial membrane is injected, often intensely so, and is granular in appearance, readily breaking down on pressure and being easily torn. Here and there small abrasions may be noticed, but they are seldom of any depth. In chronic cases the villi are thickened, and more prominent than usual; this is easily demonstrable by placing a piece in water, when the villi float up, showing their character beautifully. The peri-articular cellular tissue is affected in a similar fashion to its neighbours. All the soft tissues undergo great development of new formed tissue, and the subsequent contraction and adhesion of which, with the surrounding parts, give rise to stiffness and limitation of the joint movements, and finally to fibrous ankylosis. These adhesions and contractions play a great part in the development of deformities. On turning to the articular surfaces, we find the cartilage in the acute cases soft, with here and there an erosion, which may or may not reach the bone. In more chronic cases, besides erosions the cartilage itself may present a velvety appearance, said to be characteristic. In the bone in places will be seen small or large erosions, according to the severity of the case. In the acute cases, the bone is red, rarefied, vascular and soft, but later on becomes sclerosed, hard, dense and almost of an ivory consistency, and now there

FIG. 1.—This bone is from an acute case of rheumatoid disease. The ligaments and peri-articular tissue were much thickened, the synovial membrane was red and infected, softened, thickened and pulpy and readily broke down on handling. The cartilage as a whole was softened, and on the surface there was a small erosion about one-third of the whole of the articulating surface. There was no corresponding erosion on other cartilage. Underneath, the bone was eroded, red and soft, even extending beyond the margins of the ulcer. *Débris* filled the floor of ulcer.

may also possibly be some lipping or growth of new cartilage and bone round the edges of the articulating surfaces. Beneath the cartilage the bone presents, as a rule, a normal appearance, showing that where protected it does not undergo change. This, however, is not invariably the case, as we now and then see changes going on in bone protected by cartilage. Such are the appearances *en masse*, so now let us study the individual elements separately.

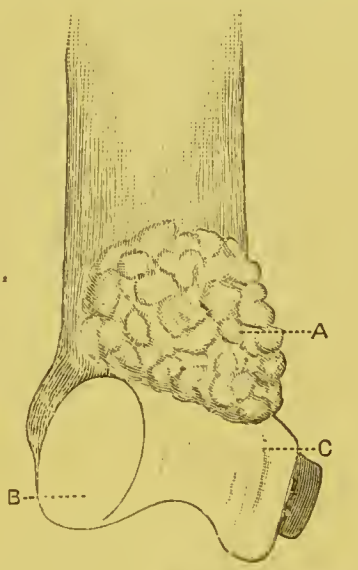


FIG. 2.—A, osteophytes; B. eburnated bone; C, Grooves on articulating surfaces (after Billroth).

2. Changes in the synovial membrane and surrounding parts.—The synovial membrane, as we have already mentioned, presents at first a bright red appearance from the injection of its vessels, is soft and pliable, but in the later stages it becomes duller, granular and hypertrophied; and, as a whole, much thickened. Lebert[13] mentions a varicose condition of the vessels of the synovial membrane, but probably he refers to a congested condition. In the later stages the villi become prominent and hypertrophied; they may undergo fatty or cartilaginous degeneration, so that the appearance may be that of a number of pedunculated fatty polypi, or else of a quantity of dendritic vegetations, villi, or fingers, some fatty, and some cartilaginous. The polypi arise from the budding and growth of the normal villi. In the normal state we know that the synovial membrane is edged by fringes and villi, and that these have appendages; and it is from these fringes that the polypi and other vegetations arise. These fringes look highly vascular, and have a soft

velvet-like feel. Under the microscope we see that the synovial cells have undergone proliferation, and that large numbers of newly formed blood-vessels exist, some full of blood, but all with thickened walls. Scattered throughout are numbers of small round cells. M.M. Cornil and Ranvier[14] state that the cartilage may be formed in the synovial fringes as follows: "The normal fat cells in the fringes or villi undergo degeneration, and are replaced by embryonic cells, and whilst those in the centre form cartilage, those at the periphery form fibrous tissue." According to Kölliker,[15] in the normal state, cartilage cells exist in the synovial fringes, and it is more reasonable to suppose that the cartilage is developed from these, than in the method suggested by M.M. Cornil and Ranvier. Rindfleisch corroborates the evidence with regard to the presence of pedunculated polypi, vegetations, villi, and fringes. As a rule these only become prominent in the chronic stages, and this specially refers to the cases where cartilaginous degeneration has occurred. The pedicles which fasten those nodules of cartilage to the synovial membrane, are apt to become stretched, and may in the end break off, giving rise to loose bodies which lie free in the cavity of the joint. In very chronic cases, these cartilaginous bodies may still further undergo change, and become ossified. It has also been stated that loose cartilaginous bodies are found in various bursæ.

The **loose bodies** found in rheumatoid arthritis may be classified into: (*a*,) Melon-seed-like bodies, and masses of coagulated fibrin, derived from the synovial surfaces; (*b*,) Loose bodies derived from the synovial membrane, consisting of fully formed tissues, such as cartilage and bone; and (*c*,) Loose bodies derived from the articular end of the bones, being detached ecchondroses and osteophytes.

(*a*,) **Melon-seed-like bodies.**—Rokitansky [15a] refers to bodies of this kind, and mentions cases in which he has seen fibrous or fibroid small bodies, varying in size and shape, projecting from the surface of the synovial membrane, and which he says can quite conceivably become detached. Again, it is stated that fibrinous exudation gives rise to both melon-seed bodies, and to fibrinous masses. A case of the latter is mentioned by Dr. Logan Turner.[55] On microscopical examination the fibrinous mass was found to consist of fibrin with a large number of cells, resembling leucocytes, entangled in its meshes.

(*b*,) **Loose bodies derived from the synovial membrane, consisting of fully formed bone or cartilage.**—Most of the loose bodies found in rheumatoid joints undoubtedly arise from abnormal development of the fringes, which normally exist at the margins of the articular cartilages. These increase in size and vascularity, giving rise to sessile and pedunculated bodies, varying in number and size. During this process the membrane itself undergoes change, and the connective tissue cells develop into fibrous tissue, fibro-cartilage, cartilage, and bone. As time goes on, the connecting pedicle of the pedunculated bodies grows thinner, and finally the body may drop off, in some cases after a slight sprain or wrench, but in others during some natural movement of the joint. These bodies, examined microscopically, present the character of hyaline cartilage, with here and there cells undergoing proliferation.

(*c*,) **Loose bodies derived from the articular ends of the bones, being detached ecchondroses and osteophytes.**—In rheumatoid joints formative changes are constantly taking place at the periphery, giving rise to nodular outgrowths of cartilage, and finally by deposition of lime salts or ossification they become bony. These

nodules may become detached possibly by injury, and thus lead to such a body existing loose in the joint. In one such case the body was found to consist of hyaline cartilage irregularly arranged. In some places it was proliferating, and in others ossification had begun.

The ligaments which form part of the affected joints become swollen and inflamed, and finally undergo absorption, or are so replaced by newly formed connective tissue, that it is impossible to trace them on the most careful dissection. Owing to the cellular tissue undergoing great development, and from the formation of new connective tissue, adhesions are formed with the surrounding parts which lead to stiffness and difficulty in moving the joint, and finally even to fibrous ankylosis.

Under the microscope the synovial membrane is seen to be infiltrated with newly formed connective tissue cells, the blood-vessels are dilated, and their walls thickened, and here and there are small collections of leucocytes surrounding them. On proper staining, micro-organisms are discovered scattered throughout the membrane, but more especially wherever there are any collections of round cells.

FIG. 3.—Diagrammatic sketch of connective tissue, showing micro-organisms (much enlarged).

Similar changes are noted in the soft periarticular connective tissue. In the ligamentous structures, during the acute stages, the intercellular spaces seem to be increased in size and number, and a few round cells present themselves; whereas, in the chronic stage, they are replaced and converted into a mass of dense connective tissue, in which little or no structure can be traced.

It has often been stated that in rheumatoid arthritis

there is no effusion. This, however, is quite incorrect, as again and again have I definitely proved its presence by tapping a joint. It certainly is present in the most acute cases, and often in considerable quantities. It is most often noticed in the knees, wrists, and phalangeal joints. In these latter joints it often forms small, tense, synovial protrusions, which give the impression of small elastic bags full of fluid. Brodie, Adams, Fuller, Garrod, Trousseau and others, have recognised the presence of fluid, whilst Besnier,[16] Senator, and Homolle,[17] deny it. On examining the fluid, Hoppe Seyler[18] found that it contained the following ingredients :—

Mucin - - - -	18·19	per thousand.
Albuminous Substances -	20·92	,,
Etherial Extracts - -	·93	,,
Alcoholic ,, - -	1·30	,,
Watery ,, - -	·65	,,
Acetic ,, - -	1·53	,,
Inorganic Substances - -	8·79	,,
		,,
Total Solids	52·31	,,
Water	947·69	,,

The etherial extracts were cholesterin, lecithin, and traces of fat. I have found the fluid to be a straw coloured viscid fluid, with a dash of reddish colouration (trace of blood), and moderately alkaline.

Under the microscope (on cold stage) large numbers of multinuclear granular corpuscles are seen, very little, if any, larger than red-blood discs. Most of the round cells are quiescent, but a considerable number of irregular ones show active amœboid movements. There are a few rouleaux of red corpuscles, and a few scattered individual red discs. Also indistinctly seen are numerous small round bodies, some highly refractile, and with them a few bodies (very faint), apparently micro-organisms. On staining these latter, they prove to be bacteria in large numbers.

Normal synovial fluid is found to contain in addition to fat molecules, a few amœboid corpuscles, as well as cells similar to those which occur on the projections of the membrane.[19] We thus see that, beyond the micro-organisms, this fluid differs also in the number of cells present, both amœboid and granular. The presence of blood is probably accidental. Dr. Goodhart, as mentioned by Dr. Fagge, on one occasion found blood effused into a rheumatoid joint.

It is very rare to have suppuration, and, in fact, I know of no case in which it has occurred. Dr. Mansel Moullin,[20] however, reports three such cases. He believes that the bacteria which caused it reached the joint by the blood. The disease in all cases began in the soft parts, and spread from thence to the bones, cartilages, and ligaments. Dr. J. R. Lunn also reports one such case.[54]

3. **Changes in the cartilages.**—Many believe that the first changes begin in the cartilages, but I am not inclined to agree with them. I think, however, that the cartilage must be involved at a very early stage. *Post-mortem*, we usually find that the whole surface of the cartilage has suffered, but, if seen early, it is also not uncommon to find the disease limited to one or more small patches. Rindfleisch says the cartilage undergoes a perfectly homologous proliferation, beginning in the outermost or superficial layers, and gradually extending to the deeper; that the cells divide, and group themselves into rows of eight to twenty, and go on growing until the matrix has disappeared, and a tissue made up of cells or large vesicles results. Billroth says the intercellular substance does not soften as in inflammation but that it breaks up into filaments. He says the changes commence in the cartilage, and spread from thence to the synovial membrane, and then to the bone and periosteum.

To the naked eye the first change is a loss of natural polish, and it comes to present an appearance which has been likened to velvet, and is softer than in the normal condition. As the disease spreads and becomes more developed, the central parts of the affected areas break down, and erosions occur which, gradually extending and deepening, cause the whole of the cartilage to be absorbed, and the heads of the bones exposed. As the erosion goes on a new formation of cartilage may take place round the edge, giving rise to the lipping or heaping up so often seen in the advanced cases. A sort of pseudo-lipping may be observed when the central portions are erosed down to the bone, whilst the marginal portions are nearly, if not quite, unaffected. Close investigation is necessary to distinguish between these conditions. When true lipping does occur, it does not do so in very regular sequence, but rather does so in nodules, and it is from this circumstance that the name "Rhumatisme Noueux," by which it was long known, was derived. Under the microscope, we find that the process of disease consists in a proliferation of the cartilage cells, beginning in the outermost or superficial layers, gradually extending to the deeper. This process was first described by M.M. Cornil and Ranvier. They show how the cells undergo multiplication, and form groups of from eight to twenty cells surrounded by capsules, and that in some cases large mother cells develop, and within these other and smaller daughter cells. Of these latter some may have their own capsules whilst others would appear to be without them.

Cornil and Ranvier show how it can be demonstrated, by staining with iodine, that these cells are not true cartilage cells, as their capsules only stain very faintly, if at all. According to them the superficial layer of capsules swells, and, becoming globular, burst, and discharge

their contents into the joint cavity. The capsules in the next and succeeding rows, being only able to grow perpendicularly, open into the more superficial rows, forming parallel tubules, and, as time goes on, these burst in turn into the joint, leaving the tubules empty (Rindfleisch and Weber [21]), whilst the ground substance or matrix lying between them becomes separated into filaments, giving rise to its fibrillated and velvety appearance. According to Rindfleisch, mucous degeneration of the fibrils occurs, causing them to disappear the more easily, and thus also explaining the presence of mucin in the joint fluid. I have never been able to verify this description.

In sections I have seen proliferation of the cartilage cells, but never any arrangement into tubules as described by Cornil and Ranvier. Did it occur, one would expect to find cartilage cells in the joint fluids. I have never done so with certainty, and I have examined many cases in the hope of finding them. Of course, the cells may have undergone so much degeneration, and alteration, that they would be unrecognizable. What I have seen under the microscope is, round an erosion, a large number of round cells which penetrate for some distance into the substance of the cartilage.

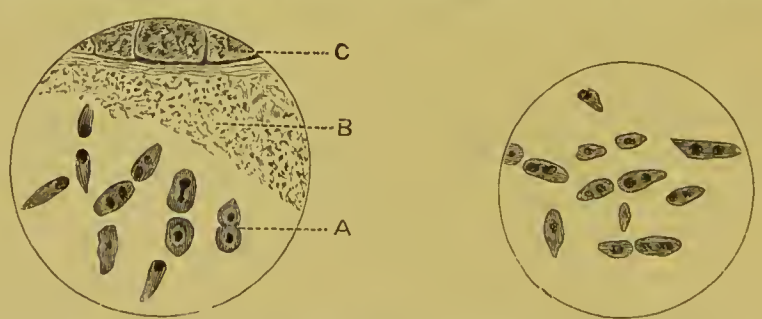


FIG. 4.—Sections through diseased cartilage; A, proliferating cartilage cells; B, round celled tissue; C, periarticular loose connective tissue.

In this area the cartilage cells are seen to be proliferating freely, and the matrix to be disappearing, being

eaten away, partly by the round cells, and partly replaced by the newly formed cartilage cells. Deeper down the proliferation still continues, but in a less marked way. With regard to the fibrillation of the matrix, the use of reagents rather interferes with one's results, so on that point I can make no definite statement, but I can emphatically state that I have never seen anything at all approaching the drawings which illustrate most of our text-books. The process is one resembling, I take it, all other erosions, and inflammatory conditions of cartilage. A few micro-organisms I have always found in the superficial layers, mixed up with the round celled tissue, also in the layer of proliferating cartilage.

The cells, at the edges of the cartilage, proliferate in a similar manner. Cornil and Ranvier ascribe the marginal overgrowth to the fact that the cartilages, at their margins, are overlapped by a layer of synovial membrane which prevents the escape of the cellular contents into the cavity of the joint. The cartilaginous overgrowth may become converted into osseous tissue, the change beginning as shown by Volkmann in the layer nearest the original bone. As a rule, even when seen in the late stages of the disease, these osteophytes have still a covering of cartilage. The lipping which is seen in gout differs from that just described. According to Dr. Wynne the outgrowths in the latter disease are a sprouting of the cancellous tissue of the epiphysis, carrying with it the cartilage, which, however, only covers it as far as its summit—the rest being covered by fibrous tissue continuous with that of the periosteum, and synovial membrane. In ossifying arthritis the lipping differs from that of rheumatoid, in that the outgrowths arise independently of the articular surfaces, and are not covered by the articular cartilages.[22]

4. **Changes in the bones.**—As the cartilage erodes, and leaves bare the bone underneath, we have certain changes occurring. In the acute stages, when the disease involves the bone, it presents a red and vascular appearance. It is soft, and readily breaks down as the bony constituents are absorbed. These are replaced by a red, semi-fluid material differing greatly from the normal marrow; and is, under the microscope, found to consist largely of giant cells, with many nuclei (osteoclasts), in a mass of round cells. As the disease becomes chronic we find the bone presents a hard, white, polished, ivory-like surface, to which the term "**eburnation**" has been applied. This hard dense layer is thin, and erosions through it, showing the cancellous tissue beneath, presenting features as above, are not uncommon.

On the surface of the exposed bone, as it hardens, we see grooves and striæ, which are found to correspond with the eminences, and protuberances, on the opposing articulating surface (see *Fig.* 2). As the result of the processes of destruction and new growth, the bones often present a mushroom-like appearance.

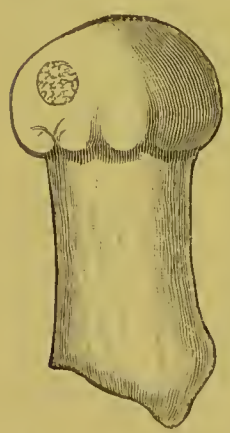


Fig. 5.—Metacarpal bone, showing osteophytes (after Billroth).

Volkmann [23] described such a condition, saying that they looked as if they had been moulded whilst in a softened condition.

True bony **ankylosis** rarely occurs, except in the spinal column (Bowlby). Adams noticed occasionally **hypertrophy** of the shafts, whilst Broca [24] described this as being chiefly confined to the epiphysis.

Various theories have been advanced to explain the **eburnation**. It is, probably, one of Nature's safeguards to prevent further inroads of the disease. Zeigler [25]

states that, whilst the superficial layers of the cartilage are proliferating, and becoming fibrillated, a softening process is going on, in the deeper layers, which leads to the formation of cavities; and these becoming filled, later on, with the vascular medullary substance which grows into them from the bone, give rise to ossification. Cornil and Ranvier believe the eburnation to be due to the discharge into the adjacent medullary spaces of the contents of the most deeply seated cartilage capsules, which, as they enlarge, cause the bone to be absorbed; and these cells from the capsules, by a process of osteosclerosis, give rise to the hardened surface. In some cases they attribute it to the extension of inflammatory processes to the most superficial layers of the bone. Some think local osteitis is the principal cause, and others that it is due entirely to mechanical means, *i.e.*, the rubbing of the bones one upon another. The bony structure of the epiphysis may also be altered.

Volkmann, whose theory is probably correct, has pointed out that the changes are caused, to his mind, by a rarefying osteitis followed by an osteosclerosis. That the wasting of the bone is not purely mechanical is proved by the fact that the change sometimes goes on in parts protected by cartilage.

On examining sections of bone, and also of the medullary tissue, it is evident that the nature of the process is a rarefying osteitis; but a process of sclerosis or hardening will be seen as the case passes from an acute to a chronic condition.

I have failed to find micro-organisms in the soft medullary tissue, but I have no doubt they exist. I find Gwilt[26] mentions that, in this disease, he noticed the medullary tissue was a great deal more vascular with proliferation of the corpuscles than in the normal. This has also been noticed by Husse[27] and Kussmaul.[28] If we

compare the medullary substance with that found in *morbus coxæ senilis*, we see that, in the latter disease, which is due almost entirely to a process of absorption, the bony interstices are filled with a yellow fatty substance, quite different from the red vascular substance of rheumatoid disease.

To recapitulate, I would say, we have an acute inflammatory disease set up by micro-organisms starting in the synovial membrane, spreading thence to the cartilage, bones, and ligaments, causing in the cartilage and bones, at first an ulcerative or eroding process, followed, as the disease becomes less acute, by hardening and thickening. This is following most other types of disease, and explains all the *post-mortem* appearances as well as all the clinical symptoms.

FIG. 6.—Osteoclast eating bone.

Before leaving this division of the subject, let us consider some other points of interest.

5. Changes in the muscles.—The principal change is a well marked atrophy of the muscle substance which affects the whole of the muscle, and not only a part of it. There is no diminution in the number of the fibres, but each fibre is found to be decreased in size. As a whole the muscle presents, what Debove [29] calls, the colour of dead leaves. In a few cases degeneration of the muscles has been found, showing itself by longitudinal striation with proliferation of the sheath nuclei, and increase of the interstitial tissue (Vallat).[30] This change, probably, only occurs in those cases in which inflammatory changes have spread from the joint to the muscles, nerves, or central nerve system.

6. Changes in the central nerve system.—The only

changes hitherto noticed have been an atrophy of the motor cells in the anterior cornua in a few isolated cases, described by Folli.[31] I have only been successful in obtaining specimens from a degenerated nervous system in one case. In this one, on examining the spinal cord, degeneration was found with vacuolation [32 and 33] of the ganglion cells of the anterior cornua. The vacuolation of nerve cells consists in the appearance, within the nerve cell, of oval or perfectly spheroidal bodies of high refractile power quite unaffected by any staining reagent, colourless, but lustrous. In many cases this quality is wanting, and it is then evident that the spheroidal outline is of a genuine cavity or vacuole from which the former contents have escaped by rupture. The removal of the contents of such vacuoles may be effected during life by absorption by the lymph connective system. The protoplasm surrounding the vacuoles is, more or less, in a state of granular degeneration. The degeneration, and the feeble staining, indicate a fatty change in the cell protoplasm. The significance of this is understood when we realize that

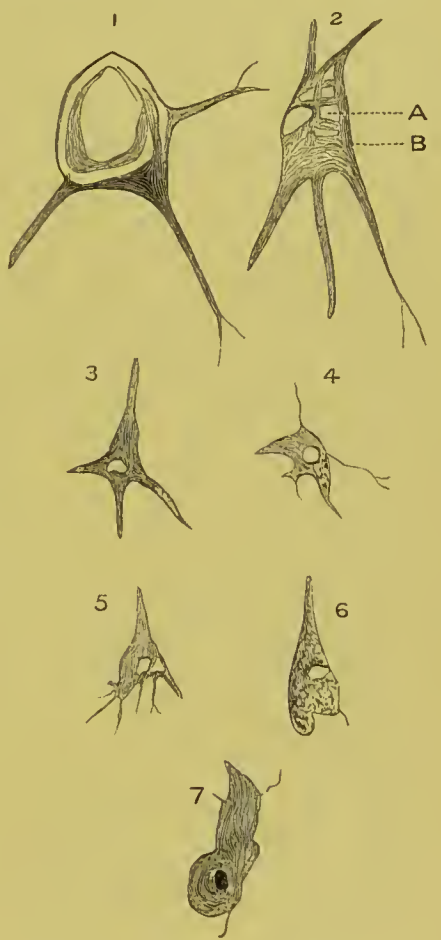


FIG. 7.—MULTIPOLAR GANGLION CELLS FROM ANTERIOR CORNUA.

× 350 { 1 Cell swollen with bright translucent contents. 2 A, Vacuoles in degenerated cell; B, Granular degeneration.

× 200 { 3 and 4 show vacuolation, seen also in 5 and 6, in degenerated cells, and 7 swollen degenerated cell.

fatty degeneration and vacuolation indicate a state of defective oxygenation, probably arising from some change in the blood corpuscles. We see examples of this in chronic pulmonary affections, alcoholic states, and from the effect of certain poisons (arsenic, phosphorus, etc.), or any of the many circumstances which restrict the supply of oxygen to the tissues. Those elements naturally suffer earliest, and most, whose nutrition is carried on at the greatest disadvantage. The exact importance of this occurrence cannot at present be accurately estimated.

Massolongo [34] refers to changes in the anterior cornua observed by Klippel, but does not particularise them.

7. Changes in the nerves.—In a certain number of cases peripheral neuritis has been noticed, but in so few as to negative any idea that this is the cause of the disease. It is almost certain that when it does occur it is caused by an extension of the inflammation of the joint. Pitrès and Vailliard [35] report some cases where they found such a condition of the nerves, but they express the opinion that these changes cannot be the cause of the joint lesions. In other cases again we find that the spinal cord and nerve roots have been affected by a spinal arthritis, probably by compression and narrowing of the foramina. In these cases we may have a descending neuritis. I have been fortunate enough to obtain sections from the nerves, in a case of rheumatoid disease which

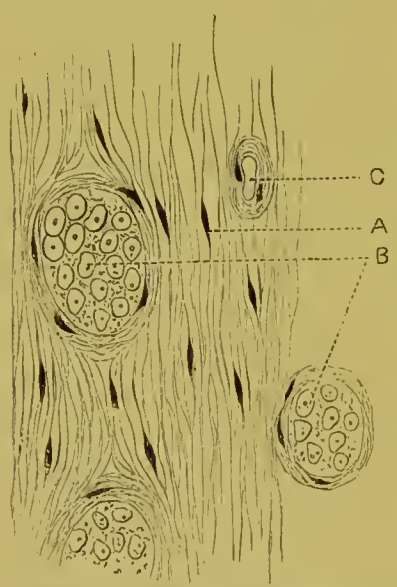


FIG. 8.—Portion of nerve in which there was neuritis; A, thickened connective tissue, nucleated; B, nerve bundles, greatly diminished in size; C, blood-vessels with thickened walls.

had undoubtedly given rise to a secondary neuritis. There could be no doubt that it was secondary in nature. Under the microscope there was an infiltration of small round cells in the nerve sheath, around the vessels, and amongst the nerve fibres themselves, especially in the neighbourhood of the sheath. Thickening of the endoneural septa, and of the interfibrillary substance, was also seen; and there was a thickening of the intima of the blood-vessels, which encroached upon the lumen of the vessel.

8. **Changes in the heart.**—Lesions of the endocardium and pericardium are comparatively rare, but not so rare as is thought. MM. Charcot and Cornil mention numerous cases in which changes were present, and with no rheumatic history, and in which the lesions developed after rheumatoid joint troubles. Any valve may be affected, but my experience has been that the disease is almost entirely confined to the mitral valves. I have had few opportunities of examining such cases *post-mortem*, but other writers state that the affected areas present a hardening, and thickening, with vascularity, and small vegetations arise from their surfaces. Pericarditis has been seen in several instances.

9. **Changes in the kidneys.**—Charcot and Trousseau lay special stress on the occurrence of chronic albuminous nephritis, but I think it is a much rarer complication than they would lead one to suppose, at least in this country.

10. **Changes in the blood.**—In almost 95 per cent. do we find anæmia exists in a greater or lesser degree. The blood, under these circumstances, presents the following characters. There is a slight, but well marked diminution in the number of red blood corpuscles, a marked diminution in the hæmoglobin, and a slight increase in the number of the white corpuscles. The percentage of

the diminution of the red corpuscles ranges from 85 to 56 per cent.; whereas that of the hæmoglobin does so from 80 to 45 per cent. It is thus evident that the hæmoglobin value of each corpuscle is lessened. The percentage increase of the white corpuscles is small. The blood shows red corpuscles of varying size and varying shapes, but does not present any microcytes nor yet any nucleated corpuscles. The hæmoglobin appears to be less in quantity in each cell, as well as in a less stable union with the cell stroma. It crystallizes out more readily and is more easily acted upon by such substances as common salt, acetic acid and sulphate of soda in solution. There is a difficulty sometimes in distinguishing between a swollen red cell with its hæmoglobin dissolved out and a white cell. This might account for the variability in the estimation of the number of the latter.

11. **Changes in the glands.**—As one would expect, we find in the glands of the arm and leg, some enlargement, but there is none of the spleen. This enlargement is such as is found in other bacterial diseases, and consists of a chronic hyperplasia. Chauffard and Ramond[36] report 7 cases in which they found enlargement of the lymphatic glands. On section these were found to be normal in appearance, except for an overgrowth of the connective tissue causing compression of the lymphoid tissue. Still,[37] describing a form of rheumatoid arthritis in children, mentions that both the lymphatics and spleen were affected. In adults I have not come across enlargement of the spleen, although I have seen it in children. In these cases, however, there were other causes which might have accounted for it, and at present I do not think much stress can be laid on this point.

12. **Fibrous nodules,** although more common in acute or chronic rheumatism, are not unknown. They consist of round celled tissue which, probably, originates in an

endarteritis. Dr. Pitt [38] describes such a condition, and mentions that this endarteritis may account for the cold extremities so often seen in this disease. Nepven [39] describes a nodule formed round a vessel with small disintegrating clots, whilst Cavafy [40] mentions that the nodules are probably vascular in origin.

A subject now crops up of much interest, namely, the relationship between chronic rheumatoid arthritis, and what are known as **Heberden's nodes.** These are small enlargements or osteophytic outgrowths from the normal nodules, round the articular surfaces of the bones of the hand. They were first described by Heberden [41] who gave it as his opinion that they had nothing whatever to do with gout. This has been, and still is, a much vexed question, and as these nodes may occur in the more chronic forms of polyarticular rheumatoid arthritis we have to ask ourselves what their relationship to this disease may be.

They occur, as I have said, as small rounded nodular growths, usually arising from the third phalanges, but sometimes from the second. They are practically painless, and have no tendency to ulcerate, and though they somewhat interfere with the movements of the fingers, yet they are more disfiguring than painful. The nodes may be the only symptom of disease present, but they are more usually associated with a generalised disease, and they may precede or follow such a disease. On examination they are found to consist of an outgrowth from the bony tissue, and are covered by a hernial process or projection of the synovial membrane, forming a pouch or bag, which, as a rule, contains fluid, and acts much as a bursa. On microscopical examination, they are found to be formed of true bone. It is found that these nodes, usually, as Heberden says, present themselves in elderly people of the female sex, above 60 years of age; but I

have seen them well developed in patients of 40. At first, we find that the third joint of a finger is enlarged, and as a whole, and not only on one aspect. On the dorsum the furrows which mark the normal joint are seen to have disappeared, and are replaced by an elevation—the whole joint forming a distinct thickening. This can be detected on the palmar aspect as well. The enlargement of the bones is not confined always to one phalanx, but both of the opposing phalanges may be affected. This enlargement goes on until we have a small tumour, obviously growing from the bone, about the size of a pea, over which glides, possibly, a bursa or synovial pouch. The development of these nodes is accompanied by peculiar sensations in the fingers, such as numbness, and they are often accompanied by pain on pressure, or on movement. They may, however, be quite painless, and even if not so, the pain is never severe. When they become quiescent the pain goes completely. If the disease is not arrested, the movements of the joints become much interfered with, and ankylosis may finally result. When nodes are present in rheumatoid arthritis we find that deformities seem to develop specially early, and to be more persistent. The usual deformity is deflection of the terminal phalanges towards the radial side, and this is rendered more conspicuous by the deflection of the finger, as a whole, to the ulnar side. Are these growths then the ordinary osteophytic outgrowths, so common in rheumatoid arthritis, or are they something different? Some assert that they are true gouty formations, and others that they have nothing whatever to do with gout, but are by nature a form of rheumatoid arthritis. Heberden, as I have said, maintained that they were not gouty, as he had seen them in people who had never been affected with gout. Begbie[42] differed from him entirely, and said they were intimately

connected with gout. He stated that he had watched their development from the first, being sometimes the result of an inflammatory affection, more or less acute, and attended with the constitutional disturbance which marks the fit of gout; but more commonly they were the consequence of a slow and chronic gouty disorder. He also said he had never seen them except in those suffering from gout or from the gouty diathesis. Charcot,[43] on the other hand, agreed with Heberden, and denied that they had any connection whatever with gout. He stated that it was a form of rheumatoid arthritis, and that the anatomical changes were those of this disease. Sir. A. B. Garrod[44] stated that he had seldom seen them in patients suffering from true gout, and agreed with Heberden's view with regard to them. Dr. A. E. Garrod[45] was of the same opinion, but said he had seen them in cases with clear histories of gout, and no other arthritic affection. Duckworth[46] believed that they were of a true gouty nature, and said that the changes found by Charcot were frequently of an undoubted gouty nature. In gout he had seen true ankylosis result from the deposit of urates, and exostoses may also be caused thereby. Lecorché[47] also took this view. Pfeiffer[48] maintained that they were a symptom of true gout, as he had seen them arise in cases of gout, and in cases where uratic deposits existed, but he admitted that he had also found them in people in whom there was no gout. Personally, I have seen these nodes most frequently in chronic rheumatoid arthritis, never in the acute forms; but I have also seen them in true gout. Is it not possible that they may be common to both diseases? They are unquestionably the result of some irritation giving rise to an increased, and morbid growth in the normal nodules; so why should not this irritation have its origin as much in the poison of one disease as in the other? I have seen a considerable number of such cases, and I

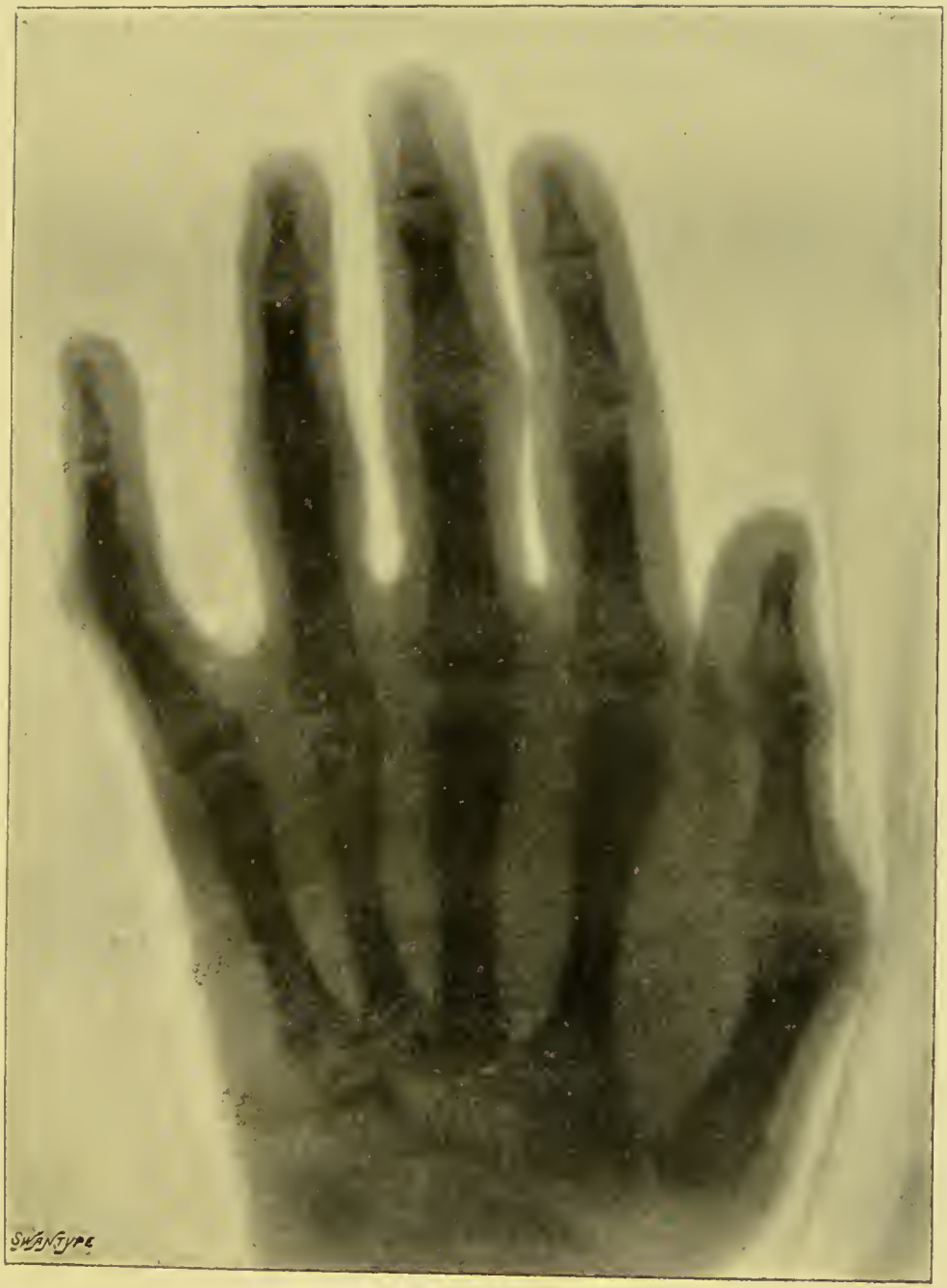
have in no instance found any deposit of gouty material in the nodules. They have always been of pure bony substance, but this, of course, does not invalidate the argument that the gouty poison may have originally started the morbid process.

The accompanying skiagraph (*Plate I*) was taken by J. W. Gifford, Esq., of Chard, the patient being an inmate of the Bath Royal Mineral Waters Hospital, and through whose kindness I am permitted to publish it.

The patient, a lad of 20, was the subject of acute rheumatoid arthritis—the synovial swellings being marked. A small sesamoid bone can be distinguished on the inner side of the first metacarpo-phalangeal joint. What is of special interest, however, is the fact, that in the acute stages no bony outgrowth occurs. Indeed, as this skiagraph shows, there is, if anything, a diminution in the size of the bone, as may be seen in the heads of the metacarpals—which have a rounded off appearance not often seen in a normal bone. This is specially noticeable in the second metacarpal at its ulnar side, the disease in this joint being specially acute. The thickened condition of the soft tissues in the neighbourhood of all the phalangeal joints should also be noted. The deformity of the little finger was due to contraction of the flexor tendons, with atony of the extensors.

Since the introduction of the X rays much has been done to show that there is no bony enlargement in the acute forms of the disease, but, as Barjon [49] shows, in the chronic stages bony excrescences are the rule. Oudin, Barthélemy, Béclère,[50] Bäumler [51] and others have all studied the disease from this standpoint, and their results are as various as the conditions examined. Most of the evidence goes to show, however, that in the acute stages no bony enlargement exists, and also that there is a

PLATE I.



Skiagraph of the Bones of the hand in a case of Rheumatoid Arthritis.

difference between a skiagraph of a tabetic knee and one of a rheumatoid knee.

Bacteriology.

For some time before the actual discovery of the micro-organisms, Dr. Wohlmann and I, looking at the clinical nature of the disease, and at the course of the symptoms, suspected that the disease was microbic in character. The absence of *post-mortem* material hindered us in obtaining any definite proof until we decided to obtain what specimens we could from the living subject. In this way we were led to aspirate affected joints, and examine the fluids so obtained microscopically and by cultivation. Now I wish it to be clearly understood in what class of case this micro-organism has been found. It has been found in only the acute polyarticular cases with soft synovial enlargements of the joints accompanied by muscular atrophy, by cold sweating palms, by pigmentary changes, by marked cachexia, by a rise in temperature, and possibly by some enlargement of the glands. I have not found it in the chronic cases with outgrowth of bone and lipping, and in fact the question arises whether we are dealing with one or two diseases. I am rather inclined to think that the name rheumatoid arthritis includes two quite distinct disorders, but for the moment I will leave this question in abeyance, as long as it is clearly understood that it was from the acute and from the acute cases only that we obtained the micro-organisms. From the joints then of acute cases we obtained some synovia, on staining which we were readily successful in determining a micro-organism was present, but at the same time were troubled with the difficulty in staining it properly, and getting the cover-glass free from precipitate. However, we, to a certain extent, overcame these difficulties, and got

fairly good results with carbo-fuchsin and methyl-blue, sufficiently so to satisfy ourselves that it was a micro-organism, and always the same micro-organism, we were dealing with. Our first culture attempts utterly failed, but by degrees we got fair results. Our apparatus and media being deficient, led in most instances to the growths dying out in the course of from three to four weeks' time. However, in the long run we succeeded in obtaining growths on blood-serum, agar-agar, and in beef bouillon. The bacillus—for to us it appeared to be a dumb-bell shaped bacillus—was found to be about 2μ long, the ends staining deeply, the connecting portion not at all. In fact in many cases it resembled a diplococcus. It appears to grow more freely when it has a plentiful supply of air, possibly pointing to a greater need of oxygen. It has also been found in pieces of synovial membrane obtained during aspiration and in the cartilages, synovial membrane, and periarticular tissues in the few sections we have been fortunate enough to obtain. On Dr. Blaxall's suggestion the blood in some of the acute cases has been examined, and in several the micro-organism has been found, but never so characteristically as to warrant one in diagnosing the disease from that alone.

The following is a synopsis of our present knowledge of the appearance, method of staining, mode of growth, etc., of the micro-organism :—

(1,) The micro-organism is very minute, appearing at first sight to be a diplococcus. The two ends of the bacillus stain deeply, but there is an intervening portion which never stains. Dr. Blaxall, after careful observation, came to the conclusion that it was a bacillus from the fact that the intervening portion is as broad as the diameter of the stained extremities, and that it has parallel contours. The average length is 2μ and the

average breadth ·6μ, varying considerably according to the intensity of the staining. Under the microscope it always appears smaller than the measurements would lead one to suppose.

(2,) The micro-organism has been found in the synovial fluid, synovial membrane, cartilage and bony *debris* in erosions as well as occasionally in the blood.

(3,) It may be stained with gentian violet, methyl violet or carbolic fuchsin. It is found, however, that these stains, if allowed to evaporate at all, deposit on the cover-glass in a manner which so closely resembles the organism that it is by no means easy to recognise which is which. The most useful stain is probably aniline-methylene blue. After fixing in the usual way the cover-glass is immersed in dilute acetic acid for about two minutes, well washed and dried, and then placed film side down on a watch-glassful of stain, and the whole placed for three to five days in a moist chamber in the dark. It is then washed in gently running water, dried and mounted. The prolonged staining deeply colours the organism, whilst the moist chamber prevents the evaporation of the dye and precipitation on the cover-glass. A still better method, and one used by Dr. Blaxall, is to mix a drop of the specimen to be examined (which I here presume is fluid) with a few drops of stain on a cover-glass, and rub out with a platinum needle. The cover-glass, with stain and synovia, is then dried slowly and passed through the flame of a burner, afterwards being freely washed, dried and mounted. It may also be detected in a hanging drop specimen. The organism very readily gives up its stain when treated with acids and other decolourising agents; by Gram's method it is completely decolourised.

(4,) On cultivation it grows best in litre or half-litre flasks of peptone beef broth which have been filtered

repeatedly until they are perfectly bright and clear. The flasks having been sterilized and proved to be so are inoculated with a drop or two of synovial fluid, and are then incubated at blood heat. During the first three days no growth appears, but on the fourth small minute particles may be seen floating in the clear fluid, giving rise to an appearance resembling "gold dust." At times the growth appears to stop at this stage, but in others it may become slightly flocculent. It never becomes turbid. A culture displays the organism, on microscopic examination, in considerable numbers either as discrete individuals or as zoogloœa masses. They are non-mobile, but have a marked oscillatory movement, as may be seen in the hanging drop specimen. Dr. Blaxall was thus enabled to watch their mode of subdivision.

It also grows on nutrient agar-agar, appearing in about three days, if kept at blood heat, as a fine transparent film, which under a lens resolves itself into minute colonies, perfectly transparent. On Löffler's serum it grows as minute points difficult to observe unless where the condensation water has washed off the cholesterin. It grows in milk without causing curdling or precipitation of the casein, but it does not grow in nutrient gelatine either at a temperature of 22° C. or 37° C.

(5,) On inoculation, experiments have been unsatisfactory. Dr. Blaxall inoculated mice, guinea-pigs and rabbits but got no fatal results, but in rabbits he suspected some joint trouble. The experiments were few in number, and as these animals do not suffer from rheumatoid arthritis naturally one would hardly expect an artificial disease to be set up. This negative result only proves that this organism is not pathogenic to the animals experimented on.

(6,) This micro-organism has not been found in any

other disease of the joints. I have examined many cases of different diseases and have failed to find it, and Dr. Blaxall examined synovia from chronic synovitis, gonorrhœal and tubercular affections, and also failed to find it.

Now with reference to the discoveries of others we have first Schüller,[52] who in 1893 described a bacillus 2·6μ long by ·75–995μ broad which exhibited polar staining, and which was easily stained by the ordinary methods, especially carbolic fuchsin, but was very easily decolourised. Growing readily on gelatine at 25° C., as small white knobs, it soon liquefied it to such an extent that the whole mass became opaque white. On agar-agar it grew as greyish-white flecks or films. It is obvious from its manner of growth that this is an entirely different organism to the one discovered by Dr. Wohlmann and myself. Bouchard and Charrin[53] described certain cases of apparent rheumatoid disease, to the French Association for Science in 1894, due to a staphylococcus, and finally, in May, 1896, Chauffard and Ramond[36] found in one case a small bacillus (diplo-bacille), short and thin, and having much the appearance of a diplococcus. It was very easily stained by all the ordinary methods, but was not decolourised by Gram's method. All cultivation experiments failed except in synovial fluid, where it grew freely. On inoculation into pigeons, rabbits, mice and guinea-pigs, they all appeared to be immune. Such is the bacteriology as it at present stands, and until definite proof can be given that the organism, found by Dr. Wohlmann and myself, can reproduce the disease, its *rôle* in the disease must remain to a certain extent conjectural. Its presence is certain, but its significance is another matter.*

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* Dr. Blaxall's report is embodied as an appendix.

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CHAPTER IV.

VARIETIES AND DIAGNOSIS.

Errors in Diagnosis — Acute Rheumatoid Arthritis — Osteo-Arthritis—Charcot's Classification—Post-Rheumatic, Gonorrheal and Gouty forms—Acute and Sub-acute Rheumatoid Arthritis — Infantile Arthritis — In Children — In Adults — Differences — Symptoms — Appearances of Joints — Chronic Rheumatoid Arthritis—Age—Appearances—Bony Changes—Diagnosis between it and Nerve Diseases—Charcot's Disease—Rheumatism—Gout—Chronic Rheumatism, etc.

1.—VARIETIES.

Probably Rheumatoid Arthritis is responsible for more errors in diagnosis than almost any other form of known disease. This not only arises from the difficulty in recognising the disease from certain forms of rheumatism and gout, but also because under the name rheumatoid arthritis several forms of disease have been, and still are classified. A further differentiation is greatly to be desired, not only on account of the treatment to be pursued, but likewise for prognostic purposes. It has been my lot to see annually a large number of cases sent to Bath for treatment, and to which, in the greater proportion of cases, the wrong name is given. Most confusion arises apparently between what is, and what is not chronic rheumatism, the larger proportion of cases thus designated being cases of rheumatoid disease; and, again, there often is confusion between rheumatoid arthritis, and some forms of chronic gout. With care one can usually differentiate between these conditions, but it is not always easy to do so straight off.

Even having settled what is recognized at present as rheumatoid arthritis a new difficulty arises, for it is not only possible, but probable, that there are at least two forms of disease included in this term. It is not quite certain that the acute polyarticular disease is the same as the chronic osteophytic and possibly monarticular one. That the later and chronic stages of the acute form closely resemble those chronic from the outset I do not doubt, yet there is a something which makes me doubt their identity. An acute case may pass into a chronic stage having most of the characteristics of one chronic from the first, but to my mind the term rheumatoid arthritis should be limited entirely to the acute polyarticular inflammatory disease, with marked wasting and trophic nerve troubles, and with no bony or cartilaginous outgrowths. When these occur the disease has invariably become chronic. For this reason it is my intention to divide the disease into two sections. In one: (*a*,) I will class all the acute and sub-acute cases characterized by inflammatory changes in the joints, and by ulceration and erosion of the cartilages and bones, by muscular atrophy, by nerve and trophic phenomena, and by glandular enlargement, etc.; and, in the other (*b*,) all the chronic cases characterized by a slowly progressive thickening and hardening of all the joint structures, by the development of deformities, by the formation of osteophytes, and by the lipping of cartilage, etc. Owing to the bony changes and to the general thickened character of the joints, it is to this form of the disease, rather than to the acuter, that I would more especially confine the term **osteo-arthritis.**

The disease may arise as a primary disease, or else secondary to such diseases as rheumatism, gout, gonorrhœa, etc. When it arises subsequent to rheumatism some observers hold that the rheumatoidal attack is merely the continuation of the rheumatic changes; but, of recent

years, other views have been advanced and accepted. We have come to understand how any acute arthritic attack lays the joint tissues open to a subsequent attack of the same disease, and also to one of some other disease. But what is curious is, that a disease originally limited to one joint should render the patient liable to a generalised disease—yet such is the case. This rather points to some blood condition, than to one entirely dependent on a local joint state. McArdle [1] points this out, and I have often proved the truth of his observation. If we believe, as I do, that both rheumatism and rheumatoid arthritis are caused by infective organisms, or by their elaborated poisons, we can more readily understand, and appreciate, the significance of this rather remarkable fact. Schüller [2] goes the length of stating that the rheumatic poison renders the joints and constitution more liable to be affected by rheumatoid arthritis. In post-rheumatic forms, we find an increased tendency to the occurrence of visceral lesions. As a sequela of gout Hutchinson [3] mentions cases as proof of his theory, as to the nature and origin of the disease. Garrod supports the view that it is a common sequela, but Sir Dyce Duckworth disagrees with it entirely. The latter holds that all deformities and distortions, met with in uratic arthritis, are due entirely to gout. With regard to their clinical features, he says, they in many ways resemble those of rheumatoid arthritis. I have failed to find any positive evidence of the onset of rheumatoid arthritis after an attack of gout, but it undoubtedly is seen in those with hereditary gouty tendencies, and who may have had obscure arthritic attacks, which may, or may not, have been gouty—more probably though they were slight but unsuspected rheumatoid warnings. The occurrence of rheumatoid changes, after a gonorrhœal arthritis, is naturally much rarer than that following a rheumatic

attack. It, however, does occur, and has been mentioned in the writings of Charcot, Lorain[4] (who gave it the name **Rhumatisme blenorrhagique á forme noueux**), Sir Alfred Garrod, Dr. A. E. Garrod, Prof. Stewart, and others.

The disease having arisen either primarily or secondary to some other trouble, is found to occur in the following sub-divisions.

I. **Acute Rheumatoid Arthritis**, and

II. **Chronic Rheumatoid** or **Osteo-Arthritis.**

For a moment, let us glance at the other forms of classification hitherto adopted—most of them being based on that of **Charcot.**[5] His was as follows :—

1. **Rhumatisme Articulaire Chronique primitif généralisé ou progressif** (the **Rhumatisme Noueux** of others).—This group included cases having a tendency to become general, the small joints of the extremities, such as those of the hand, and especially of the metacarpo-phalangeal, being symmetrically affected, and also characterized by the fact, that during the progress of the disease, most of the other joints are successively attacked in a definite order, and for the most part the mischief is irreparable.

2. **Rhumatisme Articulaire Chronique Primitif fixe ou partial.**—In this group were placed those cases in which the disease is localized to one or two of the larger joints, producing deep-seated mischief. It is sometimes called **arthrite sèche** or **morbus coxæ senilis.**

3. **Nodosities d' Heberden.** — This group contained those cases usually classed amongst gouty affections, and confined either to the extreme joints of the fingers, or else to the next row, leaving, as a rule, the metacarpo-phalangeal joints free.

More recently, Dr. Garrod[6] has qualified this classification by adding a fourth group of cases which occur

subsequently to attacks of acute rheumatism, gout, or gonorrhœal arthritis. These two classifications form the basis of all subsequent ones, and for all practical purposes are efficient, but on one point I dissent from both writers, and in fact from all English authors, and this is with regard to **Morbus Coxæ Senilis.** This form of disease, I hold, is not true rheumatoidal, and, therefore, I have omitted it from my classification. In this view I am supported by such an authority as Waldman,[7] who regards it as a purely senile change of the tissues of the joints and bone.

1.—Acute Rheumatoid Arthritis.

In this division come all cases, seen alike in the young and in the grown up, occurring either as a primary disease, or secondary to some other form of arthritis, or to injury. In these forms it is always poly-articular. Although occurring at any period of life, the acuteness of the disorder varies largely with the age of the individual attacked. In children it rarely is chronic, but tends to assume a rapidly progressive character, only differing from the acute form seen in adults by its more frequent fatal termination. In young adults it also is usually acute. In elderly people acuteness is rarely seen, but, in this respect, it makes up by its intractableness. In children, we must carefully distinguish it from those cases of multiple nerve arthropathies—a few of which have been recorded. These are so similar to what one would expect in rheumatoid disease, that I am almost tempted to believe that they are cases of this disorder, only occurring in a somewhat unusual manner. Pasteur [8] mentions such a case, in which there was no enlargement of the ends of the bones, but there was arthritis, accompanied by a hide-bound condition of the skin. Barlow [9] reports another such case, in which there were

PLATE II.

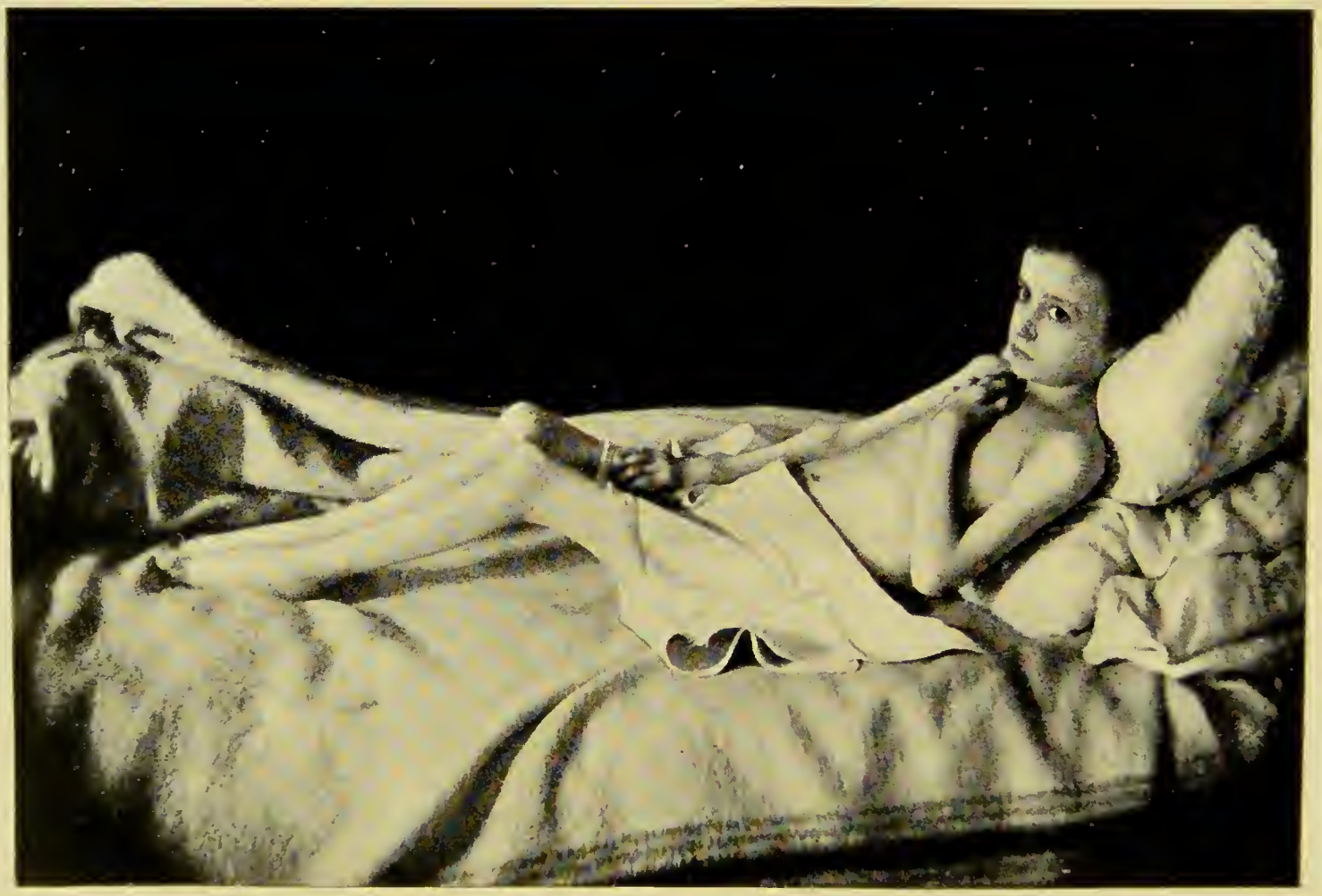
Shows swellings of wrists, knees, ankles and jaws; the swellings being soft and doughy, facies marked; also atrophy of right hand.

subcutaneous nodules. One must remember that arthritis has been known to arise in scleroderma, and scleroderma in rheumatoid arthritis. Jaccoud [10] mentions a class of cases somewhat similar, under the name of **Rhumatisme fibreux.** Wagner [11] also has described similar cases. From examinations, these joints show little change in the cartilages, but fibrous bands develop across the joints, and greatly restrict their movements, as well as lead, by slow contraction, to great deformity. There is always great doubt as to what we are dealing with in such cases, but one must always bear in mind that arthritic changes are fairly common as the result of spinal degenerative changes. Such being the case, great care is not only necessary in the diagnosis, but in the treatment. Dr. Still,[12] in Clifford Allbutt's Medicine, says there is in children a disease which presents important differences both in its clinical symptoms and morbid anatomy, as well as one which is clinically analogous to the rheumatoid arthritis of adults. The first type of disease is characterized by chronic progressive enlargement of the joints, with enlarged glands and spleen. The onset is acute with pyrexia, and the joint thickening affects the tissues round the joints, rather than the bones or cartilages, and there is also muscular wasting. Enlargement of the glands is a constant symptom, and in 9 out of 12 cases the spleen was also enlarged. *Post-mortem*, the synovial membrane was thickened and vascular, and there was some pitting of the cartilage, but there was no osteophytic change. The pure rheumatoid arthritis in children he considers to be characterized by bony thickening and lipping about the joints, and by the presence of bony grating and the absence of enlargement of the glands and spleen. Now his description of the first class corresponds to my description of what we see in adults in the acute form of the disease,

and also his second with the chronic form. To me he appears to be considering just the self same forms of the disease. I do not believe that the first form he describes as peculiar to children differs in any respect from the acute form in adults except in the splenic enlargement, which may have been an accidental occurrence so common in children; but of course the question still remains, Are there two diseases both in adults and in children? Dr. Still's idea of what is pure rheumatoid arthritis is the popular one, that there must be bony enlargement. This, I would strongly urge on my readers, is not the case, at least, not in the forms we most frequently see it in in Bath. The youngest child I have seen affected was a boy, aged four, the next, also a boy, aged seven (*Plate II*), and the next a girl, aged eight (*Plate III*). Undoubted cases have been recorded by Sir Alfred Garrod,[13] Lecaze Dori,[14] Monocoro,[15] Dr. A. E. Garrod, Lloyd Davies,[16] etc. In his "Diseases of Children," Dr. Money[17] mentions that rheumatoid arthritis is seen in children, and that it may follow on an acute attack of rheumatism: that it may affect both the feet and hands, and resemble the multiple joint affection of middle-aged women, rather than the arthritis sicca of the old. The propensity, he says, to deformities and ankylosis in awkward positions is rather great. Henoch, in his book on "Diseases of Children," also mentions certain cases of apparent rheumatoid disease, but he, like many foreign observers, does not differentiate between it and chronic rheumatic arthritis.

Turning to the consideration of the acute form as seen in adults we find Fuller[18] was the first to point out its characteristics and subsequently Garrod drew attention to it, pointing out various things to be noted in the differential diagnosis between it and acute rheumatism.

PLATE III.



This shows well the swellings in fingers, wrists, knees, jaws, etc.; also the peculiar facies and general emaciation.

PLATE IV.

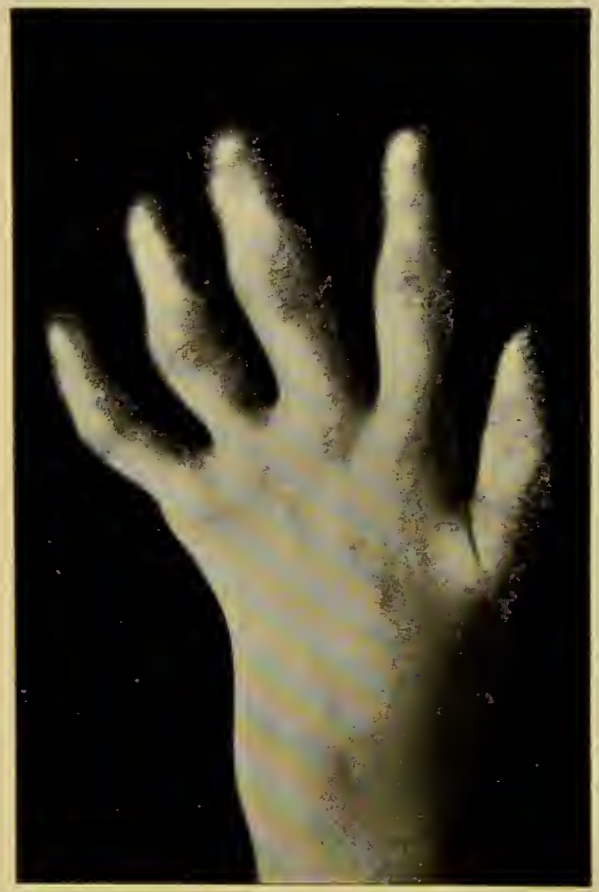


Fig. A.—Spindle shaped enlargement of joints with marked atrophy.

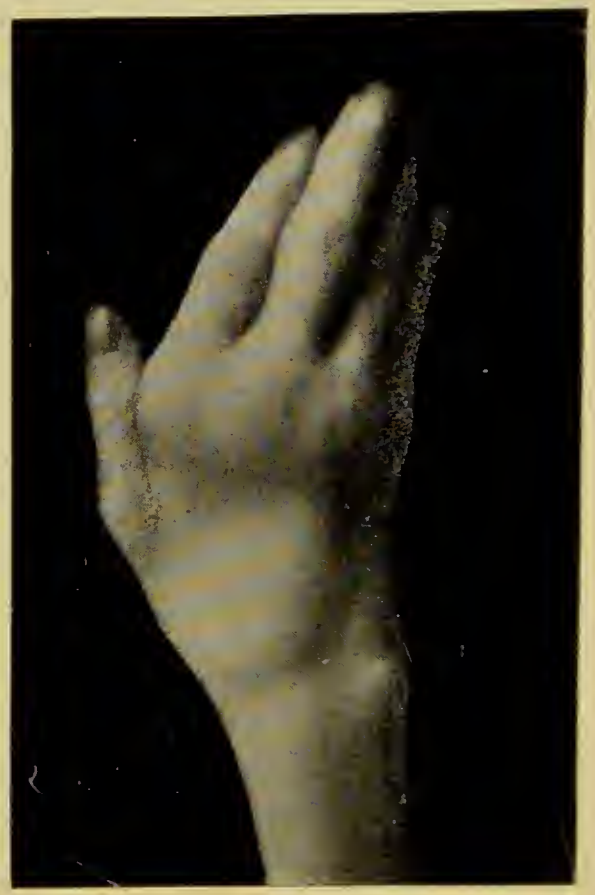


Fig. B.—Pulpy swelling of joints.

Both he and Fuller draw attention to its obstinacy, to the character of its articular swellings, and to the liability of certain joints to be involved. Some deny that this form exists, holding that it is only a modification of acute rheumatism, but, although, if care be not exercised it lends itself to much confusion, yet, to one who has studied the two diseases, no confusion is possible. In rheumatoid arthritis the disease involves the bones, cartilages, synovial membrane, and ligaments, and is accompanied by well marked atrophy, trophic, vaso-motor, and other nerve phenomena, which render it quite distinctive and characteristic.

It is undoubtedly more important from the clinical standpoint than the average chronic case, and what makes these cases so specially interesting is the age at which they occur, children and young adults being for the most part affected. We find it usually commences in one joint, probably one of the metacarpo-phalangeal ones, but it does not remain long confined to this one joint, but spreads like wild-fire to most of the other joints of the body. It shows a wonderful symmetry not only in the joints affected, but, to a less extent in the degree. Symmetry is also seen in the other phenomena present. The joints are swollen, presenting a characteristic, ovoid or spindle-shaped enlargement, painful and tender to the touch, and hot. On palpation, they either feel resistant and elastic (*Plate IV, Fig. A*), with distinct fluctuation, or else they feel as if they had undergone maceration. The ligaments and other joint structures being soft, and doughy, and admitting of a finger tip being sunk between the heads of the bones; and they at times feel as if they would drop apart (*Plate IV, Fig. B*). The second condition is the more advanced stage of a rapidly progressive disease—the cartilages, and other joint

structures, being destroyed by the acute inflammatory process which is at work. Later on the joints will become harder again as cicatrisation and condensation occur. This feeling, and that of tense resistance, are quite characteristic. Along with this the extremities feel cold, and look blue, being bathed in a cold clammy perspiration, although the body temperature is raised generally. Recent pigmentations, and other integumentary abnormalities, develop on the face, body, and forearms, etc., and enlargement of the glands is seen, whilst all the time a progressive muscular atrophy is occurring. The affected muscles are not merely those in the immediate neighbourhood of the diseased joints, or even distal to them, but may be situated on the proximal side as well. A characteristic selection of the muscles is observed, the atrophy is accompanied by cramps, and fibrillary twitchings, with, sometimes, increase of the reflexes, but, unless peripheral neuritis has been set up, no reaction of degeneration. As the case progresses the pain becomes greater, worse probably at night, and on movement of the joint; the movement also gradually becomes more and more limited. No sleep may be obtainable, except by the use of powerful hypnotics, and the disease becomes more and more distressing to watch and to treat. Cardiac abnormalities are fairly common, whilst pleurisy, pneumonia, or pericarditis may add their quota of distress to an already overtaxed system.

II.—Chronic Rheumatoid Arthritis or Osteo-Arthritis.

In this form it may be only the later stages of an acute attack, or it may arise *per se*, and be always chronic; or it may follow on some other form of arthritis; or as the result of injury. It may affect many joints, or it may be confined to only one or two. As a

primary disease it is most often seen in middle-aged and elderly women. It is characterized by great hardening and thickening of the joint tissues, both soft and hard; by eburnation of bone; by erosion of the cartilages; by osteophytic deposits; by cartilaginous overgrowths and new deposits; by lipping, etc. There is consequently much deformity, distortion, and stiffness. This latter varies, as in one case it may be of the slightest, whilst in another it may resist all treatment, and end in ankylosis. Pain as a rule is not acute, being more of a constant, gnawing, or wearying character. One joint only may be affected, and in which it may remain, or it may advance steadily from joint to joint, causing great crippling, not only from deformity, but from fixing and ankylosis. One marked feature is the absence of fever, of almost all heat in the joints, and by the absence of the trophic and gland changes. It looks as if the sclerosis or condensation of the bones and tissues, so peculiar to this condition, had given them power to resist not only the inroads of the micro-organisms, but the absorption of their toxins. We must in these cases discount all the trophic and nerve abnormalities of the acuter stages and those arising from disuse. In many respects in rheumatoid arthritis one sees resemblances to phthisis, but in none more so than between the acute and chronic forms, for, have we not an almost analogous condition between phthisis and fibroid phthisis?

2.—DIAGNOSIS.

From **Charcot's Joint Disease** it may be distinguished clinically, by the absence of the nerve symptoms so well marked in that disease, especially the muscular incoordination, etc., and by the fact that the joint changes in tabes are marked by the suddenness of the onset; by

the absence of pain; by the large quantity of fluid in the joint; by the fact that the joint changes at first are always atrophic, although they may later on become hypertrophic, and by the increased mobility.

From other **nerve arthropathies** by the absence in them of pain, and by the presence of well marked nerve symptoms.

From **Syringomyelia,** by the formation of new bone in rheumatoid arthritis being confined to the interior of the joint capsule, while in syringomyelia and other spinal arthropathies there may be extreme ossification of the periarticular soft parts (Volkmann). This cannot be relied upon, however, as in the chronic cases of rheumatoid arthritis there may be considerable formation of bone in the adjacent tendons, ligaments, bursæ, etc., but the paralysis, ocular and bulbar, should, if carefully noted, render the diagnosis fairly easy.

From **Pulmonary Hypertrophic Osteo-arthropathy,** by the presence of pulmonary troubles in that disease, and by the changes being almost entirely confined to the bones, more especially their shafts, but until more is known of this disease we are not in a favourable position to lay down strict laws with regard to its differential diagnosis.

From **Acute Rheumatism** there is little difficulty in making a diagnosis, except in those rare cases of rheumatoid arthritis, where several joints become acutely inflamed at one time. The whole history of the case is otherwise different. Its preponderating frequency in women is a point of importance. Apart from this, the general clinical features of the arthritis are quite different; while acute rheumatism begins in the medium sized joints and spreads to the smaller, rheumatoid arthritis begins in the smaller and spreads to the larger. The former, too, is migratory and uncertain in

its extension; the latter is slowly progressive, with a greater tendency to symmetry. The pyrexia of acute rheumatism, the perspiration, the greater liability to cardiac complications, are all characteristic. The real difficulties arise in chronic cases, when the joint must be minutely examined so as to make out that the stiffness, swelling, and deformity, depend upon a general thickening of the textures about the joints, and not on destructive changes in the joint.

From **Chronic Gout** the distinction is made by noting the previous history, and by careful examination of the joints. Besides the fact of its greater frequency in men in middle life, whose habits and mode of life contribute to bring it on, there is usually an account of previous acute attacks in the joints, mostly the great toe, and, while in the course of time other joints are affected, the disease cannot be said to have the same progressive character and symmetrical spread. The joint changes too are different. Urate of soda deposits may be noticed in, or about the joint, as well as elsewhere, as in the ears, etc. What is quite certain is that the destruction of inter-articular cartilage, and alterations in the ends of the bones in rheumatoid disease, are not due to previous gouty deposits.

A point to be noted in diagnosis is the muscular atrophy, which presents in rheumatoid arthritis the following peculiar and typical features:—

1. It is most marked in the muscles in the immediate neighbourhood of the joints (interossei, etc.).

2. It is not infrequently found to have affected muscles beyond this region (trapezius, deltoid pectorals, etc.).

3. It improves, and tends to disappear if the joint trouble ceases, although it would seem to persist at times long afterwards.

4. It is sometimes accompanied by changes in the electrical excitability of the muscles.

In all cases also the teeth should be examined. In gout they are almost invariably ground down—even in women, whilst in rheumatoid arthritis this is never seen unless in people with a gouty inheritance.

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Table Showing Differential Diagnosis.

	Acute Rheumatoid Arthritis.	Chronic Rheumatoid Arthritis.	Acute Rheumatism.	Chronic Rheumatism.	Gout.
1	Inflammation quickly involves cartilages, but does not give rise to lipping or bony outgrowths.	Is characterized by great new formation of bony and cartilaginous tissue.	Affects only the fibrous tissues, and is marked by great synovial distension, pain and heat.	Has little tendency to the destruction of the joint tissues, and no tendency to the formation of bony and cartilaginous deposits.	Inflammatory thickening of the joint tissues, with deposits of Urate of Sodium, but does not tend to destroy tissues.
2	Joints affected permanently; deformities not so common.	Joints once affected are so permanently; deformities common.	Usually in a more or less transitory fashion.	———	———
3	Most common in females and the young.	Most common in females.	———	———	Most common in men.
4	Is a fairly acute disorder.	Does not run an acute course.	Is an acute febrile disease.	Is not acute	May, or may not be acute.
5	Usually hands bathed in cold perspiration.	———	Is accompanied by sour swelling perspiration.	———	———
6	Heart and lung complications fairly common.	———	Cardiac lesions very common.	———	———
7	Marked muscular atrophy and many trophic phenomena, glands enlarged.	Muscular atrophy and trophic phenomena not so marked.	———	———	———
8	———	———	———	———	Uric acid always present, either in blood or deposited in tissues.
9	Is specially liable to affect neck, small joints, and jaw symmetrically.	Symmetry not so marked.	Does not affect neck and jaw as a rule, and symmetry not so marked.	No symmetry as a rule.	Chiefly affects great toe; no symmetry.
10	———	———	———	———	Teeth ground down.

CHAPTER V.

SYMPTOMS AND PROGNOSIS.

Premonitory Symptoms—Spender—Primary Symptoms due to Micro-organisms—Appearance of Joints—Heat of Skin—Arthrite Sèche—Synovial Pouches—Joints first affected—Symmetry—Ankylosis—Deformities—Dislocations—Osteophytic Out-growths—Forms of the Deformities—In the Hands and Knees—Its Causes—Difference in Acute and Chronic Cases—Cardiac Symptoms—Endocarditis—Pericarditis—Changes in the Glands—Secondary Symptoms—Muscular Atrophy—Its Characters—Selective Power—Myotatic Irritability—Fever—Pulse Rate—Tachycardia—Tension—Anæmia—Hæmorrhages—Purpura—Neuritis—Its Frequency—Trophic Phenomena—Skin Changes—Glossy Skin—Loss of Hair—Atrophy—Downy growth of Hair—Pigmentation—Sweating—Dyspepsia—Kidney—Cardiac troubles—Prognosis.

1.—Symptoms.

As a rule, in every illness we find some salient, constant and characteristic abnormalities which may be taken to represent an individual disorder. It is so in rheumatoid arthritis. In this disease the joint symptoms are characteristic and constant, and the character and number of them, with the number of the structures attacked, all suggest a systemic disease.

The symptoms may be divided into

A.—Premonitory Symptoms;

B.—Primary Symptoms, and

C.—Secondary Symptoms, being those more especially due to the absorption of the bacterial products.

A.—The Premonitory Symptoms.

The disease, in many cases, has no premonitory symptoms, the first indication of anything being wrong being slight pain in a joint with some swelling, and

tenderness on pressure, or on movement. Should, however, premonitory symptoms be present, they usually present themselves in the form of numbness, tingling, or other abnormal nerve sensation of the extremities. Howard,[1] Homolle,[2] and Garrod,[3] all mention such cases. Howard compares them with the abnormal sensations noticed in spinal disease. Garrod quotes cases in which there was a sensation of pins and needles in the arms and hands, and growing pains in the bones. In my experience I have never been able to get a really reliable history of any such premonitory symptom. I have had patients say they have felt abnormal sensations, but on further investigation there has almost invariably been some antecedent trouble which has caused such confusion as to render the evidence quite unreliable. Patients naturally pay more attention to slight abnormal nerve sensations than they do to a trivial pain or swelling of a finger joint or knuckle. I think, therefore, little reliance can be placed on the occurrence of premonitory symptoms. Before leaving the subject, however, I would mention the symptoms described by Dr. Spender,[4] which, according to him, if not actually premonitory, occur very early after the onset of the disease. The symptoms referred to are various vaso-motor and trophic disturbances, which will be discussed more fully later on, and pain. The pain on which he lays such stress is one occurring in the ball of the thumb, and on the inner side of the wrist. He considers it to be of great importance, and almost pathognomonic, and it may be accompanied by a feeling, described by patients, as of being "parboiled, scalded, stung all over with nettles," etc., the pains themselves being various in character, but those of a neuralgic character being most common and characteristic. They are more often referred to the bones than to the joints themselves.

Given then a disease ushered in by the foregoing premonitory sensations, or by neuralgic pains, it is not long before we find evidence of the disease in the joints themselves; and, following on the joint symptoms, come atrophy of the muscles, with, at shorter or longer intervals, certain other symptoms due, for the most part, to derangement of the nerve and vaso-motor systems. The occurrence of certain changes in the joints, with or without these other symptoms, then, constitutes the disease called rheumatoid arthritis. Of the local symptoms, of course, the most important are those referable to the joints.

B.—Primary or essential Symptoms.

1. Symptoms due to the presence of micro-organisms in the joints.—To the eye the earliest symptom is some enlargement of one or more joints. This may vary in degree from the most trivial swelling to an enormous distension. It assumes all sorts of shapes and characteristics, and the skin covering the joints may be subject to many and various changes. Apart from trophic changes it may be reddened, but more often presents a bluish, asphyxiated look quite characteristic. As a rule, the shape is more or less characteristic in so far as the joint alone is affected, but should the tendons or their sheaths have undergone rheumatoid change, one can never say what the alteration may be. In an ordinary acute case the joint will be more or less spindle-shaped, merging gradually into the tissues above and below (*Plate V, Fig. B,* and *Plate IV, Fig. A*), due either to the presence of fluid, or else to pulpy swelling of the synovial membrane; occasionally we may find that the swelling is not symmetrically spindle-shaped, and there are what seem to be pseudo-depressions between the heads of the bones, due to these latter being pushed apart by the swollen joint tissue, and to the general

PLATE V.

Fig. A.—Shows deflection of left hand. There is complete dislocation of 1st phalanx of index finger on to palmar surface of metacarpal, and partial of 2nd phalanx on to palmar surface of 1st ring finger.

Fig. B. Shows spindle shaped swelling of phalangeal joints.

softening of the ligaments and tendons (*Plate III, Fig. B*). In chronic cases the enlargement is usually more irregular, and may, from the enlargement of the heads of the bones, and from the presence of nodules of osteophytic growth, as well as from the swelling of the synovial membrane and presence of fluid, present an enormous and irregular enlargement. As the disease commences in the synovial membrane it is not until the later stages of the acute, or in the chronic form that we see much bony enlargement *(Plate VI, Fig. A)*. Owing to cystic enlargements, or bursæ, certain aspects of the joint may be increased in size out of all proportion to the rest. In many cases the mapping out of the synovial sacs is very perfect, from the swelling being almost entirely confined to them, and, in such cases, the enlargement is sharply demarcated from the surrounding tissues.

While the acute stage is still in progress, to the touch the joints feel hot — the temperature often being raised 1°–2° Fahr. above that of the surrounding surfaces.

As to the eye, so to the touch, we find three conditions:—

(*a*,) A tense, elastic, and resistant swelling with distinct fluctuation, often with secondary sac-like protrusions of synovial membrane—best seen in the joints of the fingers, and evidently caused by the presence of a considerable quantity of fluid under some tension.

(*b*,) A soft flabby doughy enlargement, feeling as if the joints, ligaments, and all the surrounding tissue had undergone maceration. Over the joint cavity there may be a sort of depression in the middle of the otherwise generalised swelling, and everything feels doughy or pulpy. There is seldom much fluid present in such cases, but the swelling being due to the dis-

organization and pulpy synovial membrane they are most acutely progressive. It is often a late stage of the acute form, and shows that much destruction of the joint has taken place.

(*c*,) The third condition is that described by the French under the name, "Arthrite Sèche." In these cases the joints are enlarged and nodular, and one feels that the heads of the bones have undergone enlargement; the synovial membrane is doughy; there is much crepitation on movement; movement is difficult and this even, if passive, causes pain; and there may be ankylosis. It is not seen in the more acute stages.

At first, on passive movement, there may be little or no pain, and there may be no tenderness; but pain in the acute forms soon becomes marked and persistent both on movement and at rest, especially at night. On movement in the drier, and more chronic forms, we get grating on moving the heads of the bones one over another. This may become quite a marked feature. At first it is of a fine character, but soon passes into the coarser varieties of crepitation, which convey the idea that one is rubbing two erosed pieces of bone together, and which only cease from total inability to move the joint.

During the first stages the skin over the joints may be reddened, and dusky in hue, with increase of pigment, etc., whilst in the later we see various trophic changes, such as "glossy" skin.

With regard to the pouches or cysts seen either in connection with, or in proximity to, a joint, Mr. Morant Baker[5] says that they arise from the synovial cavities by a process of distention. The synovial fluid on reaching a certain degree of tension finds its way out into the tissues in the direction of least resistance. It does so either through some normal channel, such as

PLATE VI.

Fig. A.—Shows cartilaginous and bony enlargements of the heads of the bones, with considerable synovial swelling and thickening. Atrophy is marked. K—Shows thickening of wrist joint.

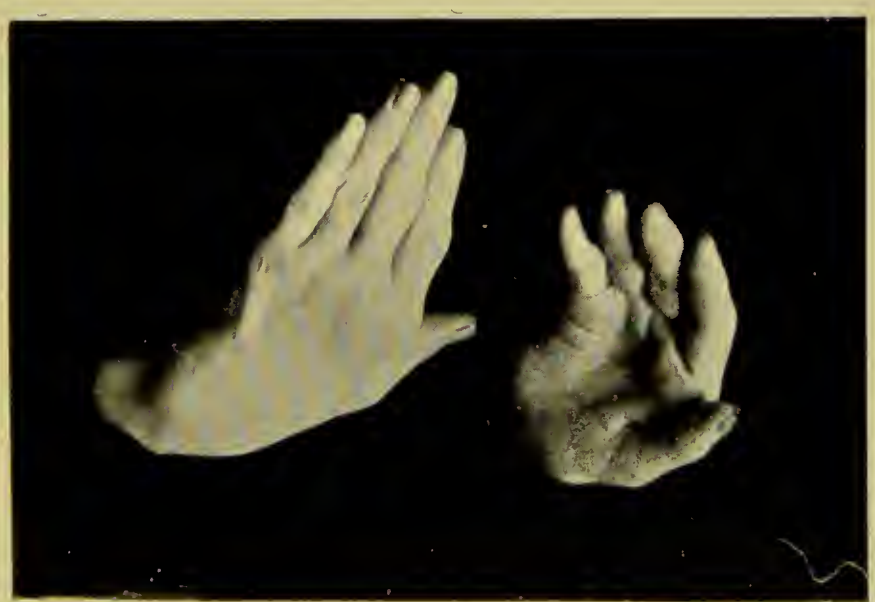

Fig. B.—Ulnar deflection in a chronic case.

that by which a bursa communicates with a joint, or else by the formation of a hernial projection of synovial membrane. Finally it pushes its way into, and between, the tissues until its boundaries come to be formed by the muscles and other surrounding tissues. I have often watched such pouches gradually being pushed through the tissues surrounding the joints, and one can readily understand how they might have their communication with the joint cut off either by pressure, from a rapid enlargement of the joint, or else by a twist, or by some inflammatory process. I do not think that these synovial pouches ever actually burst. On puncturing them I have, more than once, seen the escape of all the fluid from a joint; and, on pressure, one can make them disappear with a temporary increase of the fluid in the joint, thus demonstrating their intimate connection with it.

With regard to the presence of fluid in the joints: in almost all the acute cases it is present, often in large amount. However, with the synovial membrane and ligaments in a state of doughy or pulpy softening and degeneration, it is not always easy to differentiate between the two conditions. Hæmorrhages into the joints are rare, but not altogether unknown. Suppuration is even rarer, and I have never seen it (see p. 64).

In the acute forms of rheumatoid arthritis the small joints of the hand are those most liable to be affected by the rheumatoid changes. They are usually the joints first affected, and often form the starting point from which it spreads all over the body. It not infrequently happens, however, that the disease is not only confined to the fingers, but to the terminal interphalangeal, or even one terminal interphalangeal joint.

Charcot gives the following statistics from 45 cases, as to its origin[6]:—

25, or 53·5	per cent.,	started in the small joints of the hands and feet first.
4, or 8·8	,,	started in the great toe first.
7, or 17·7	,,	started in the hands and feet at the same time as in a larger joint.
9, or 20·0	,,	started in the larger joints first.

He says the arthritis, as a rule, spreads from the periphery to the centre; the fingers first being affected, then the elbows, and then the shoulders. In young patients he says it is usually general from the first, and that it is only in the elderly or chronic cases that its progressive character is so well seen. Haygarth[7] mentions that 20 out of 34 cases had the hands affected first, and Ord[8] 24 out of 38. Garrod out of 500 found that 252 commenced in the hands, 64 in the knees, and 28 in the feet; whilst in 430, or 86 per cent., the hands were affected at the same period of the disease.

In the 293 cases I take for comparison, I could only get a reliable history in 230 with regard to the joint first affected. Out of these, 68 per cent. began in the hands; 16 per cent. in the ankles; 10 per cent. in the knees; 4 per cent. in the shoulders, and neck; and 2 per cent. in the elbows and hips.

The disease rarely, or never, travels down a limb, although it may occasionally do so from a knee or elbow to the fingers or toes. It is noticed that the joints most liable to other conditions are those most liable to be affected also in this complaint, with one exception. This is the temporo-maxillary joint, which is rarely affected in other disorders, but shows a peculiar liability, almost pathognomonic, to be affected in rheumatoid disease. It may happen that the disease in the jaws is so extreme that all movement is prevented, and feeding has to be effected through the vacant space left by the

removal of a tooth. The inability to open the jaw may only be from stiffness and cicatricial contraction, but it may also happen from true ankylosis.

Garrod gives a table of the joints most frequently affected. For comparison, I also give my results :—

						Garrod's Percentage.
Out of 293 cases	97·4	per cent.	had their	hands	affected ...	86·0
,, ,, ,,	84·6	,,	,,	elbows	,, ...	25·0
,, ,, ,,	82·0	,,	,,	neck	,, ...	—
,, ,, ,,	73·0	,,	,,	knees	,, ...	60·6
,, ,, ,,	67·9	,,	,,	ankles	,, ...	34·4
,, ,, ,,	67·9	,,	,,	jaws	,, ...	25·0
,, ,, ,,	61·9	,,	,,	shoulders	,, ...	25·0
,, ,, ,,	12·5	,,	,,	hips	,, ...	14·6
,, ,, ,,	2·5	,,	,,	sterno-clavicular		—

The centripetal order is broken at the neck and knees, but as these joints are specially liable to arthritic trouble we would almost expect them to be so also in this disease. In acute rheumatism, the knees are the joints most frequently affected. One of the most marked features of the disorder is its **symmetry**. This is not only seen with regard to the joints affected, but also to the time of the invasion, and, to a less extent, to the degree of severity with which individual joints are affected. At the same time it is usual to find one limb more affected than the other, and the peripheral joints more than the more central ones. This is often beautifully demonstrated. Garrod says this symmetry is carried so far that corresponding portions of the cartilages are destroyed. This I cannot confirm. Dr. Havilland Hall [43] recently mentioned that the crico-arytenoid joint may be implicated in this disease. Bearing in mind how generalised the disease is, there is no reason why the arytenoid cartilages should escape, more especially as the neighbouring joint, the temporo-maxillary, is so often affected, and Casselberry [44] has recorded a case the clinical history

of which would point to the crico-arytenoid joint being thus implicated.

When **ankylosis** occurs it may be from true or fibrous ankylosis, or more rarely from interlockings of the osteophytic out-growths. This latter is most common in the case of the jaws. Fibrous ankylosis may usually be diagnosed from true or bony ankylosis, by some slight movement detected on careful examination, or the attempt to obtain movement may cause a contraction of the muscles which oppose it, or else pain may be induced. Spondylitis, or disease of the vertebræ, is not uncommon, and it is confined almost entirely to the acute form.

In all cases, at one time or another, there is **pain**. The pain is varied, and arises from many different causes. That arising in the joints is, as a rule, of a gnawing character, is made worse by movement, and often by the warmth of the bed. It differs in intensity in different cases, and from time to time. Although there may be no actual pain in the joints, patients often complain of a pain in the ligaments and tendons, as if the joints were being stretched. Pain is usually less in the joints distended with fluid, but in acute cases with comparatively little effusion, and where the eroded cartilages rub one on another, it is most marked. Besides this we may have pain from cramp or spasm of the muscles, or there may be pain referable to the bones. Again, we may have neuralgic pains ; and pain along the course of a nerve, due to neuritis. In some cases there may be radiating pains which, if there be spondylitis, is probably due to irritation or compression of the nerve roots.

We now have to consider the **deformities** and **dislocations** which may arise in chronic cases and apart from synovial thickening. In every joint affection there is a certain amount of deformity or distortion due to the thickening and swelling of the joint tissues, and possibly in rheu-

PLATE VII

Fig. A.—Dislocation backwards of index finger through relaxation of ligaments and erosion of the cartilages and head of the bones; also partial dislocation of ring finger.

Fig. B.—Shows ulnar deflection.

matoid arthritis it may stop at this stage, but, on the other hand, as the disease progresses, and as the tissues become contracted, destroyed, or greatly weakened, there may arise those great alterations from the normal which cause so much crippling and distortion. The disease, as it advances, may cause an increased tonicity on the part of certain muscles, and a weakness, or atony, on the part of others, the result being a deformity which, although at first readily reducible, soon becomes irreducible and permanent. Along with the development of such deformities we find marked wasting, and shortening of certain muscles, which may occur to such an extent that joints quite free from disease may actually become partially or completely dislocated. This has also been known to occur in such diseases as paralysis agitans, congenital brain atrophy, etc. (*Plate VII, Fig. A*), where the process is of course very slow, and chronic in its nature. A somewhat similar condition has been described by Jaccoud,[9] as occurring in his "Rhumatisme fibreux." It may also occur in all chronic forms of arthritis.

In rheumatoid arthritis the principal deformities are seen in the hands and knees. The deformities of the hand occur in two ways. There may be deflection to the ulnar or radial side, or there may be extension or flexion. A combination of these two types is what we most commonly see. The disease having commenced in the fingers, spreads in course of time to the knuckles and wrists. These become large and nodular, and, probably, at the same time some deflection of the fingers occurs. This may either be ulnar, when the whole of the finger is involved, or else radial, when only the terminal phalangeal joint is affected. This radial deflection of the terminal joint has been explained, by some, as being due to osteophytic outgrowths on the ulnar side. The ulnar deflection only takes place from the metacarpo-

phalangeal joints, and, except for radial deflection of the terminal joints, any deformity of the phalangeal joints is usually confined to a fusiform enlargement arising from synovial thickening (see *Plate VII, Fig. B*, and *Plate VIII, Fig. A*). When, however, the knuckles have become affected the fingers may begin to deflect from these joints, but always to the ulnar side. At first easily reducible, the deformity rapidly becomes irreducible. The deformities are brought about principally and primarily by relaxation of the ligaments and tendons. Herringham suggests that it may be caused by atrophy of the abductor indicis, and by the then unsupported finger pushing the others to the ulnar side. Duckworth[10] points out that such atrophy is not a constant feature, and this therefore has to be discounted. Pure atrophy alone will not cause it.

As a rule the thumb escapes, if the terminal joints alone are affected, but it suffers if the disease becomes more general. As the wrist enlarges the natural shape of the arm and forearm is lost, and it comes to appear as if the limb from the elbow to the wrist were of the same thickness. One often notices that the bursæ in the neighbourhood of the olecranon are enlarged, and it is fairly common to find that cartilaginous bodies have developed in these bursæ. In the larger joints it is usually impossible to find any deflection. The deformities arise in a similar manner in the feet, but are less common.

Under the second type we find deformities of flexion or extension. They were first described and classified by Charcot,[11] who divided them into two main types, with several sub-varieties :—

I.—The first form is that most often met with. It is marked by

(*a*,) Flexion of the terminal phalanges on the second at an obtuse, right, or even an acute angle.

(*b*,) Extension of the second phalanges on the first.

(*c*,) Flexion of the first phalanges on the metacarpals.

(*d*,) Flexion, to a less obtuse angle, of the metacarpals and carpals on the bones of the forearm.

(*e*,) In a great many cases, inclination of all the fingers to the ulnar border of the hand.

The sub-varieties are:—

(*a*,) The first and second phalanges being in the same axis, form a single column, with the other characters as the main type.

(*b*,) The terminal phalanges are extended on the second, and the backs of the fingers appear excavated beyond the prominent heads of the metacarpal bones.

II.—The second type is characterized by

(*a*,) Extension of the terminals on the second phalanges.

(*b*,) Flexion of the second on the first phalanges.

(*c*,) Extension of the first phalanges on the metacarpals.

(*d*,) More or less marked flexion of the carpals on the bones of the forearm.

(*e*,) In some cases deviation of all the fingers towards the ulnar border of the hand.

The sub-varieties are:—

(*a*,) Flexion of all the segments of the hand, except the terminals, on one another, so as to appear rolled up.

(*b*,) Is similar, except that there is extension of the second on the first as well.

With regard to the thumb, it is usually flexed, but occasionally it is found extended. Combined with these changes there is usually flexion of the elbows, pronation of the forearm, rigidity of the shoulder, and the upper limb is fixed on the chest. Garrod makes the flexion or extension of the middle joints the basis of his classification, and which, therefore, necessitates the inclusion of

the second sub-variety of the flexion type as a sub-variety of the extension type.

With regard to the lower limbs the hips usually remain mobile, but the knees are flexed and fixed.

Charcot says that the chief deformities are as follows:—

(*a*,) The lower end of the femur projects in front of the head of the tibia;

(*b*,) The internal condyle becomes more prominent;

(*c*,) The patella, thrown outwards, rests on the outer condyle;

(*d*,) The head of the fibula projects externally.

In the tibio-tarsal joint ankylosis is common. The foot is, as a rule, abducted, and rests on its inner edge. The big toe is turned outwards, so as to cover the other toes. With regard to the cervical vertebræ one often sees the head thrown forwards, and bent on the sternum, so as almost to let the chin touch it. The neck is widened posteriorly.

If we now turn to the deformities of the knee joints, we see that the joint is almost invariably flexed, and mayhap slightly rotated. Can we account for this in any way? In disease of the condyles of the femur we know the leg always assumes a flexed position to a greater or less extent, and that, after flexion, the foot rotates out, and rotation increases the flexion. In diseases of the synovial sac, unattended by disease of the condyles, cartilages, lateral or crucial ligaments, the entire joint remains straight. In diseases of the entire joint, including the cartilages, the leg always flexes, whether there is fluid present or not. I must qualify these propositions by mentioning that certain pathological changes may modify these deformities. But such exceptional deformities are always easily accounted for, as, for instance, that seen in Charcot's disease, or in cases

attended by complete destruction of either condyle of either side of the tibia. Many have tried to account for flexion upon the fluid hypothesis. It is true that when the knee-joint is forcibly injected it will flex slightly, to give the greatest possible capacity to the capsule, but this is insufficient to explain the deformities. The fluid hypothesis is wrong, because in, by far, the largest percentage of cases, there is no fluid effusion, and large serous effusions are often unaccompanied by flexion, and after a joint is evacuated in large effusions it does not resume the straight position. These are valid reasons why the fluid hypothesis is incorrect. But let us now examine a knee-joint. It is a hinge which, when in the straight position, is firmly fixed, owing to the tension of the lateral and crucial ligaments. This forces the articular surfaces firmly together and prevents lateral motion. The leg flexed, there is lateral motion of the joint, which increases as the leg flexes, and not only lateral but rotary motion takes place. This is due to the relaxation of the crucial and lateral ligaments by flexion. Another fact; the patella, and a portion of the capsule anteriorly receive their nerve-supply from the obturator, and probably from the anterior crural. The other portion of the joint is supplied from the great sciatic. The great sciatic supplies the flexor group, while the obturator and anterior crural supply the extensor group. A clinical fact is, that when the entire joint is attacked with acute inflammation, all the muscles surrounding it are affected by spasm. Still flexion rapidly takes place, whereas disease of the condyles always produces great spasm and rapid atrophy of the flexors, while the extensors remain quiescent. Diseases limited to the patella produce spasm and atrophy of the quadriceps extensor femoris.

In rheumatoid arthritis, we find certain muscles pre-

senting a weakness (usually to extension), resulting from an atrophic condition, and others (usually the flexors) a condition of increased tonicity. The result is naturally flexion, and, as the limb flexes, rotation follows, and we have the deformity so commonly seen. The increased tonicity arises probably from reflex irritation from the joint, or else by the action of the toxins on the governing nerve cells.

The question has been raised, How do the deformities, looking at them as a whole, arise? Some have held that they arose from an intentional desire to lessen the pain. Trastour,[12] and Beau,[13] were both of this opinion. Charcot held that they were due entirely to muscular contraction, spasmodic if not convulsive. These spasms are caused according to him by a reflex action due to irritation in the joints. This view was also taken by Crocq. Nowadays it is recognised that they arise from the weakness of one set of muscles being more than overcome by the strength of another set. In the lower leg and foot we may instance the long flexors, extensors, and interossei as being specially affected. These latter flex the first row of phalanges, and extend the second, thus accounting for many of the deformities. When they are strong we have deformities of the extensor, and, when weak, of the flexor type. It must not be forgotten, however, that there are accessory causes such as the weight of the limbs, and a more or less decided laxity of the ligaments. The deformities are not exclusively the property of rheumatoid arthritis (and in fact are not so very common in it in the acute form), but may occur in gout, chronic rheumatic arthritis, paralysis agitans, etc.

Dislocations.—We find that dislocations either partial or complete arise from the lengthening of certain ligaments, due to a softening or disorganising process, combined with an increased tonicity of certain muscles; whilst

the opposing ones have undergone atony. Dislocations may also arise from severe and extensive ulceration of the heads of the bones. We find that the most common dislocations are those of the knees, wrists, and fingers. In the case of the knee, the tibia is most often dislocated backwards, the wrist either backwards or forwards, and the fingers on to the palmar aspect, the distal bones being displaced under the proximal ones through the anterior ligaments giving way (see *Plate V, Fig. A*).

In chronic cases, the deformities are much more marked than in the acute, and dislocations also occur more frequently. The most usual type is dislocation of the wrist and fingers forwards. These dislocations and deformities become more pronounced as the disease advances, and as contraction of the cicatricial tissue takes place. In cases, chronic from the first, they are less pronounced, partly owing to the osteophytic growths. It has been noticed that a hand which is used, up to the last, does not develop such a regular type of deformity as another, which has been kept at rest.

2. Symptoms due to the presence of micro-organisms in the blood.

(a,) **Cardiac conditions.**—I must now touch on a much vexed question, namely, the occurrence of cardiac lesions during the course of the disease. Personally, I am of the opinion that endocarditis and pericarditis, especially the former, are much more common complications than one would expect. The former is fairly often seen, but the latter much more rarely (in only about 4 to 5 per cent.). Charcot says that they occur pretty frequently, and present the same characters as are seen in acute rheumatism. They are usually seen in the acute stages or during an exacerbation. To him they appear to be less grave than those of acute rheumatism. He gives instances of these lesions being found *post-mortem*. Romberg,[14] Todd,[15]

Trastour,[16] Beau,[17] and Ball,[18] all mention cases in which they have found cardiac lesions with rheumatoid disease. Besnier [19] took this view also, but declared that they are rare. Sir A. Garrod [20] does not believe that they ever occur, and Dr. A. E. Garrod supports him, although admitting that cases are seen with cardiac lesions, due, he thinks, to some previous rheumatic condition.

Out of 293 cases, I found 17·9 per cent. suffered from cardiac conditions which had developed since the onset of the rheumatoid attack.

In several others there were cardiac conditions, but the history in these cases not being perfectly clear they were ignored. Numerous cases occur in hospital work in which undoubted acute endocarditis and pericarditis have developed during the period they were under observation. Given a micro-organism circulating in the blood, it is of course probable that we will have symptoms referable to their growth on the endocardium and pericardium. As I have said, the cardiac lesions, except in the case of the pericardium, are seldom of a very extensive nature, and, in the majority of cases, I have found the mitral valve to be the one most likely to be affected—the other valves less often. Clinically they give rise to a booming systolic murmur rather characteristic. Pericarditis is often severe and extreme.

(b,) **Changes in the glands, etc.**—In a considerable number of cases we find enlargement of certain glands, especially in children (Still,[40] Playfair [41]), most commonly those in the groins and armpits. In a few rare cases I have found a chain of glands running up from an affected joint. They invariably are found on the proximal side of an affected joint. The glands are usually enlarged in size, from that of a hazel nut up to that of a walnut, and are painful on pressure, the pain

shooting up and down the limb, but otherwise giving rise to no symptoms. I have never, as yet, found an enlarged spleen.

(c,) **Fibroid nodules and fibrinous exudations** occur in rheumatoid disease as well as in rheumatism, syphilis, etc. The former are seen chiefly in adults, are chronic in nature, are often painful and tender, and vary much in size and shape. They are found in the subcutaneous tissues, and often close to a joint. Their occurrence has been noted by Howard,[21] Payne,[22] Duckworth,[23] Pitt,[24] etc. If we hold that these nodules consist of a central necrotic area, surrounded by dense connective tissue and cell exudation, there can be only one possible explanation. The bacilli circulating in the blood must have caused an endarteritis, with cell exudation and inflammation, which, if severe, has ended in a local necrosis.

Extensive fibrinous exudation giving rise to a hide-bound condition of the skin has been noted by Jaccoud and Pitt. The exudation in these cases much resembles granulation tissue.

C.—Secondary symptoms, or those due to the absorption of the bacterial poisons.

1. Of these secondary symptoms, the principal may be referred to the **muscular system.** In all acute cases we have a certain amount of **muscular atrophy** developing sooner or later. It is one of the earliest and most persistent of symptoms, but may vary greatly in degree. In some it is so slight as almost to be imperceptible, whereas in others the joint trouble seems quite secondary to that of the muscles affected. One of its peculiarities is a selection of the muscles affected. It is noticed, as a rule, that the extensors and interossei are peculiarly liable, but not invariably so. One muscle only or a whole set of muscles may be affected, and yet the form and extent of the disease in the joints would

appear to have little effect on this phenomenon of selection. It is this selection, and the increase of the tendon reflexes, which prove that the changes are not entirely due to disuse. For we must remember that prolonged disuse will give rise to an arthritis, combined with muscular atrophy, having many of the symptoms of a rheumatoidal one. Such cases have been mentioned by Bonnet,[25] and Tessier.[26] The selective character of the atrophy, in rheumatoid disease, is peculiar, and this we see when we compare it with what occurs in alcoholic muscular atrophy, where the extensors chiefly are affected, especially of the legs; with lead, where it is the extensors of the fingers and wrist; and with diphtheria, where it is the muscles of the throat, and internal muscles of the eye that suffer most. It is still more remarkable that the selective power of toxic agents should exert itself on the motor filaments only, or on the sensory ones, as well as on them both together. Indeed, in some cases there is good ground for supposing that even the trophic and vaso-motor nerves may be specially picked out. With regard to this point, we must bear in mind that in the diseases mentioned, we have to do with a peripheral neuritis, but in rheumatoid arthritis it is probably a central disturbance which is responsible. The reflexes vary in different cases, but in a pure case of rheumatoid they are usually slightly increased. This would rather point to some irritative lesion somewhere. It is possible that the slight changes seen in the reaction of degeneration indicate a difference between an intoxication and a degeneration. I am inclined to think so. In the cases where the reflexes are absent it is almost certain that we have to do with a neuritis, probably set up by the joint inflammation or by toxins, or it may even be due to a descending degeneration. In the case of a neuritis, there will probably be pain along the course of the

affected nerve, and there will also be other characteristic signs. The atrophy, as we see it clinically, has been said to be of different kinds: (*a*,) either due to a neuritis arising as is stated above; but (*b*,) more commonly it is attributed to some reflex nerve influence having its origin in the peripheral nerves of the affected joints; and (*c*,) since the discovery of the micro-organism, I hope it will be generally conceded that it arises more probably from some toxic nutritional condition of the ganglion cells of the anterior cornua of the spinal cord. With regard to this question Gowers[27] points out that the atrophy from disuse is trifling, and tardy, and affects the muscles of the diseased limb as a whole; and that the whole limb being affected, precludes the possibility of the atrophy being due to any local inflammatory change. He further points out that the changes are such as frequently result from degenerative changes in the pyramidal tracts, due to changes in the terminations of the pyramidal fibres in the gray matter. As a further proof that it does not arise from a local change is the fact that the whole of a muscle is affected, and not only that part immediately in contact with, or distal to, the affected joint. To cause this atrophy by peripheral means, the irritation must be intense; but I would much rather believe that it is caused by a local agent circulating in the blood, such as a toxin affecting the afore-mentioned centre. The atrophy resembles that occurring in other forms of arthritic muscular atrophy, not only in its distribution, with its increased myotatic irritability, but also in the absence of any reaction of degeneration. Should any neuritis have occurred, of course we will get the reaction of degeneration. Fibrillary twitchings have been occasionally observed in the wasted muscles. A tendency to spasm occurs with the increased myotatic irritability. This spasm may exist for hours, and give rise to the most acute pain, usually having a

cramp-like character. Ballet[28] mentions cases accompanied by chronic spasm which occurred paroxysmally.

2. Symptoms due to changes in the **circulatory system.**

The circulatory symptoms are various, and some of them will be considered when we come to the nervous system.

(a,) **Fever.**—The general body temperature seldom shows much rise, but in the acute stages there is always fever, usually of an irregular type. It seldom is high, but, on one occasion, I have seen it as high as 105° Fah. That it rises nightly during the more progressive stages, I have no doubt, but owing to its irregularity, and from the fact that it is seldom high it is usually overlooked. One reason assigned in chronic cases for the want of fever is that owing to the condensation of the joint tissues the absorption of the toxins is very slow, and no great quantity is absorbed at once. This, I think, is hardly a sufficient explanation. Most of my hospital cases, where accurate observations are taken, present a certain rise every evening of from one to four degrees, and this may go on for months, as a rule, quite unsuspected both by the patient and by the medical attendant, unless attention be specially drawn to it.

Amongst the other symptoms we have *(b,)* **Tachycardia** or increase of the heart rate. Sir Dyce Duckworth first pointed out that palpitation in this disease was not uncommon. An increase in the pulse rate was also pointed out by Charcot,[29] but it was probably not until Spender[30] drew attention to it, that any special significance was placed on this. Spender says, that in the acute cases the greater number are characterized, from the beginning, by an increased velocity and tension of the heart's action, and the pulse may go up at once to between 80 and 90,

and remain so for years. He says, "we are startled by counting a steady pulse of much tension, varying from 90 to 110 . . . . . The pulse quickens synchronously with the earliest sign of osteo-arthritis; there is a gradual rise until the numerical frequency of 110, 115, or 120 is reached, and there is scarcely any physiological variation during day or night . . . . . the body is absolutely non-pyrexial, and the icy purple coldness of the hands is often a striking fact. There is no hæmic murmur, and there are no signs of the heart being in any way affected. The acceleration of the circulation is not paroxysmal, the phenomenon does not belong to that group lately described by Dr. Bristowe,[31] in which the rate of pulsation now and then suddenly increases, and as suddenly lessens, nor is there any sign of venous engorgement or of local œdema. It is as if the heart were running along without check; as if the inhibitory power of the pneumogastric nerve were partially withdrawn, or partially neutralised by a cerebral influence which cannot at present be defined." Such, in his own words, is the condition which he describes. I am afraid I cannot altogether support him in his observation. It is undoubted that we all see cases of rheumatoid arthritis with an increased pulse rate, but cannot this be accounted for by the fact that in most cases there is some pyrexia, and by the fact that most patients with rheumatoid disease are undoubtedly neurotic. Sit down quietly by the patient's bedside, and you will find that a pulse, going at the rate of 120, or over, will gradually subside and diminish in frequency. Such at least has been my experience in a large proportion of cases. But, now and then, we undoubtedly come across cases corresponding in all essentials to those described by Dr. Spender. They are, however, not very common. The tachycardia probably arises from the cardiac nerves and centres having

come under the same influences which affect so many of the other portions of the nerve system.

We now turn to another class in which (*c*,) **Anæmia** occurs. Although resembling many other anæmias in being secondary and symptomatic in nature rather than primary or idiopathic, that of rheumatoid arthritis is none the less interesting; and in its details may be classed with those forms seen in various other infective diseases. We seldom find it very marked except in advanced and very acute cases, but in all, even the slightest, there is, as a rule, a certain amount of blood deficiency. Roughly speaking in about 95 per cent. of the cases presenting themselves, in all stages, do we find it to a greater or lesser degree. We rarely find extreme pallor of the skin, the patients presenting more often a sallow or brownish yellow complexion, with moderate blanching of the mucous membranes. This sallowness may, by degrees, pass into deeper shades, until it insensibly merges into a distinct discolouration. Not infrequently is it accompanied by functional cardiac bruits and venous hums. Hæmorrhages, so common in other anæmias, are rare, but not unknown. They are very rare from the mucous membranes, being most commonly seen as small purpuric spots on the legs. I have seen it two or three times as hæmatemesis and hæmoptysis, and once under the nails of the fingers and toes. Of course hæmorrhages are rare, as they mostly occur in cases where there is 50 per cent. or more blood deficiency and where it depends more on a diminution of the corpuscles than on that of the hæmoglobin.

(d,) **Hæmorrhages.**—Purpuric hæmorrhages are usually small and are usually subcutaneous. They almost never occur from the mucous and synovial membranes. Hæmatemesis I have seen several times, and hæmoptysis once.

PLATE VIII.

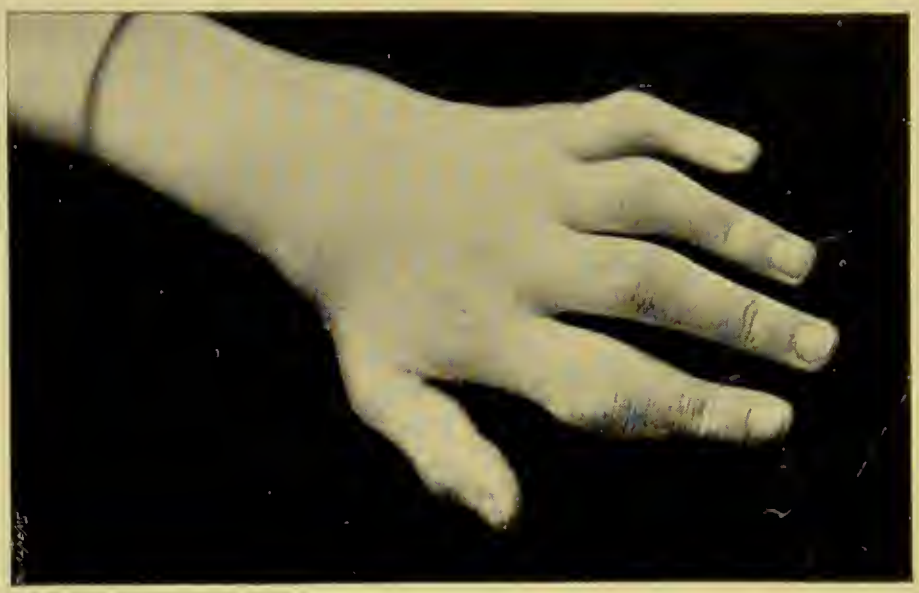

Fig. A.—Shows fusiform deformity of index finger.

Fig. B.—Haemorrhage under nails in Rheumatoid Arthritis.

In the course of a year I have, on an average, seen perhaps six or eight cases where purpura was well marked, the hæmorrhagic effusions usually occurring on the front of the legs, and more rarely on the forearms. A very interesting case was one where it had occurred under the nails of both hands and feet, before admission. When first seen it was beginning to clear up, but showed as a brownish discolouration under the nails. The accompanying photograph (*Plate VIII, Fig. B*), shows the lesion during the process of clearing up. The hæmorrhages are almost undoubtedly due to the rheumatoidal toxic poison inducing anæmia with dilatation of the blood-vessels and extravasation of their contents.

(e,) **Angio-neurotic œdema** has been noticed in rheumatoid disease as occurring in patches, often near a joint, but usually near a joint not affected by the disease. It is usually characterized by some burning and pricking and by itching.[43]

3. Symptoms due to abnormalities of the **nervous system.** Now, although strictly speaking almost all, if not all, the secondary symptoms are due to derangement of the nervous system, yet I have chosen for obvious reasons to describe them separately under the various systems in which they occur, leaving only neuritis and the more miscellaneous trophic changes to be considered under this heading.

(*a*,) **Neuritis** is a fairly common complication, and usually arises from inflammation spreading from the joint to the nerves in the proximity, more rarely from the effect of toxins on the nerves themselves. Its most prominent symptom is pain along the course of the nerve, with atrophy of one or more muscles. This may become extreme. Faradic irritability is lost, but that to voltaism is increased in amount and often, but not always, altered in

quality. In slight cases the increase of voltaic irritability may be trifling. In the nerves the irritability to both currents lessens and is ultimately lost. There is a tendency for it to spread to other branches, and nerves, and to gradually affect nearly all the muscles of the limb. Muscle-reflex action (myotatic irritability) is invariably lost. The muscles in these cases are paler than normal and smaller in bulk. The fibres are reduced in size, and are pale in colour; the transverse striation may be preserved or they may be granular; and the nuclei of their sheaths and interstitial tissue may be increased in number. These cases differ much from the ordinary cases of rheumatoid arthritis, and often give rise to difficulty in arriving at a diagnosis.

Apart from the direct spread of inflammation from the joints to the nerves, the neuritis may be caused by the poison generated by the micro-organisms. Recent researches prove that it is these poisons, and not the organisms themselves, that act on the nerves. The fact of symmetry helps to prove that it is a cause acting through the blood, and the selective action as seen is also typical of the action of toxic agents upon various parts of the nervous system.

(b,) **Other trophic phenomena.**—We best see that some disturbance of the trophic function of the nerves has taken place, from the symptoms due to vaso-motor disturbance. It is probably due to this that we have those cold clammy blue hands, evidently a local asphyxia, with sweating of the palms, pigmentation, etc. Along with these, but more rarely, we see local erythema and congestion. Occasionally distinct areas of atrophy of the skin have been observed; perhaps one of the most marked and most common forms being that known as "**glossy skin.**" This condition was first described by Paget, and more recently by Mitchell. The skin, in this condition,

looks as if it had been varnished, and much resembles a chilblain on a big scale, or else a highly polished scar. The hairs for the most part disappear. The affected skin is smooth, hairless, almost devoid of wrinkles, pink in colour, and glossy. In contra-distinction to this we often see a recent growth of downy hair, especially on the forearms. Again, we may see a condition of **scleroderma**. In this condition we have patches of skin, white and ivory-like, indurated, and stiffened, and as if frozen. The skin may be bound down to the tissues underneath, and may impede movement, and cause deformity; the papillæ of the skin being flattened, the cutis thinner than usual, and composed of more homogeneous connective tissue, and the skin as a whole is less fibrous than in the normal. The hairs gradually disappear until a condition of alopecia is observed. Along with this atrophic condition a certain amount of chronic inflammation is seen, as evidenced by the abundant nuclei in the altered skin, principally around the vessels, and sebaceous glands, and in the rete Malpighii. Œdema of the subcutaneous tissues, especially of the legs, has been observed by Vidal,[32] and Charcot,[33] unaccompanied, however, by any cause which would ordinarily give rise to it. The nails may become brittle, and deeply ridged in the longitudinal directions. Hadden[34] has described ulcerations of the fingers, and wasting of the soft parts is pretty common. Fagge[35] mentions cases in which fibrous nodules occurred some distance away from the diseased joints, as in the muscles of the arms and forearms. They must be distinguished from ordinary rheumatic nodules. Colombel[36] also mentions various trophic changes, especially of the skin.

4. Abnormalities of the **integumentary system.**

(*a*,) Increase in the **chromatogenous** functions of the skin. Dr. Spender[37] first drew attention to this.

phenomenon. The pigmentation varies from light yellow to a deep bronze colour, and it may occur in small freckles, or in large blotches. It is most usually seen on the forehead, temples, eyelids, hands, forearms, or front of the legs. The freckles are round as a rule, sharply defined from the neighbouring skin, are not raised, but have a tendency to symmetry. When they occur as blotches they are darker in colour, and are not so symmetrical, except on the face, where they often surround the eyes, involving the eyelids and spreading out on to the forehead. The onset and clearing up of these pigmentations can often be watched if the patient be kept under careful surveillance for some period of time, and are of use as giving some indication of the patient's condition.

(b,) **Sweating.**—In most cases at one time or another we see abnormal sweating. It may be a mere dampness, or else it may be so excessive as to make the skin wringing wet. It may be limited to one portion of the body, such as the palms of the hands, soles of the feet, face, or forehead, or it may be general. Although dripping with perspiration, yet the patient's skin feels cold, and almost deathlike, and they always complain of coldness of the extremities. These are blue or of an unnatural whiteness.

5.—The symptoms referable to the **alimentary tract** are probably of less significance and are more of the nature of a complication than those of the other systems, but still in the large proportion of cases we find some alimentary derangement. This usually takes the form of gastric disturbance, accompanied by flatulence, and acid eructations. The bowels are almost always confined, and there is sometimes a tendency to vomiting. The importance of these disorders is appreciated when we know that most of our treatment now-a-days is directed to improv-

ing the patient's general health, and to assist in the elimination of toxic products, a thing we cannot do if the digestive arrangements are out of order. It is also of importance to remember that this may be the route through which the micro-organism gains its access to the system generally.

The urine is as a rule normal, but in some cases Money[38] found excess of urea and uric acid, and occasionally transitory glycosuria. This excess of uric acid is denied by most authors, and I have never found it. Drackmann[39] noted a diminution of the phosphates excreted; Böcker found a diminution of phosphate of calcium in the urine, but there was four times as much found in the blood.

Apart from the cardiac conditions the principal visceral complications are due to the occurrence of such diseases as pneumonia, bronchitis, phthisis, interstitial nephritis, etc. Sclerotitis, iritis, and conjunctivitis occasionally occur. Deafness, due to the ossicles of the ear being affected, and aphonia, due to the implication of the arytenoid cartilages, sometimes are seen. Certain skin affections, apart from those already mentioned, such as psoriasis, have been described as occurring in rheumatoid arthritis, but their presence is probably nothing more than an accidental occurrence.

II.—Prognosis.

With regard to prognosis little can be said of an encouraging nature, if we look forward to a perfect cure. Once a joint is destroyed, as it rapidly is, we can never make it as of old. Cases seen early may be completely cured, but once destruction of the cartilages has occurred I see no possibility of this occurring. One can subdue the acute stages, but still we have left the hardening, and thickening, the pain, stiffness, difficulty of movement, and a certain amount of crippling. Still it

is marvellous what can be done, and I would never say that any case is absolutely hopeless, for by care and proper treatment the pain can be alleviated, and life made more bearable both to the patients themselves and their immediate companions. At the worst, the complaint is rarely fatal to life; but what is life if one is a total cripple, a trial to one's self and to all about one? On the whole I would say that the hope, to make the joint, or joints, as good as they originally were, is futile—it cannot be done, but we can relieve pain, subdue the destructive elements, and leave only the actual joint changes to be combatted. These are no small mercies, and, in the near future, we may hope for even greater successes. One warning I would give, and it is, take the disease in time, take it in its earlier stages, and you will reap an adequate reward in the relief you have obtained for the sufferer, and in the knowledge that you have subdued what has hitherto been regarded as an altogether incurable complaint.

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CHAPTER VI.

TREATMENT.

Preliminary considerations—Antitoxin—Causes—Diet—Clothing—Exercise—Drugs—Creasote—Guaiacol—Guaiacol Carbonate—Benzosol—Phenols—β-Naphthol—Betol—Salol—Action of Creasote—Hudeod—Douglas Powell—Intestinal Antiseptics—Iron—Arsenic—Iodides—Salicylates—Actæa Racemosa—Ichthyol—Hyoscyamus—Relief of pain—Dr. Spender's treatment—Guaiacol externally—Carbolic Acid applications—Electricity—Thermal treatment—Alkaline and Sulphur Waters—Bath—Aachen—Action of Bath Waters—Bath treatment—Aix treatment—Hot Air Baths—Sea Voyages—Extension—Excision—Summary.

Until quite recently, certain forms of Rheumatoid Arthritis have been regarded as not only quite incurable, but also almost impossible to alleviate. So far from this being the case, I believe all cases, if recognised early, are curable, and if, in the later stages, not curable, yet the attack can be arrested, and further damage prevented. When much disorganization of the tissues, soft and hard, of a joint has already taken place we of course cannot renew them, and make them as of old, but we can arrest its spread, and we can alleviate suffering, and by improving the general health, give greater ease and comfort—in fact, the activity of the disease being subdued we have only the permanent destruction and disorganization left to deal with. This has been brought about partly by our better comprehension of the nature of the disease, and partly by newer methods of treatment. Now that we know it is a parasitic disease, our way becomes clearer, and we have, at last, a definite aim in our methods and

modes of treatment. The discovery of micro-organisms as a cause is too recent for us to have yet found an antidote, but I am in hopes that before long one, having as powerful an effect for good, as that of diphtheria, will be found. As the question of immunity depends on the neutralization of the bacterial toxins the actual destruction of the bacteria is a secondary matter to the discovery of some chemical agent having neutralizing power. Meanwhile, and until we obtain the necessary agent, we have to content ourselves with some of the newer drugs with antiseptic and eliminative properties: and these in conjunction with dietetic and thermal treatment have yielded such remarkable results that I consider the future full of promise. I am speaking of pure cases of rheumatoid disease, and not of "Malum coxæ senilis," a most important fact to remember.

Before considering the treatment proper, it is of importance to bear in mind that one of the first considerations which any medical man, called upon to treat this affection, must deal with, is the cause or lesion through which the poison has gained access to the blood. In this respect it differs from those diseases of which diphtheria is a type, in that, in them, the disease can be attacked at the seat of inoculation; whereas, in intra-joint disease the organism can only be sustained while it elaborates its antitoxins, and marshals its leucocytes to do battle with the invading legions of inimical micro-organisms. During the course of treatment one must carefully guard against anything likely to lower or debilitate the system. The importance of this is understood when we remember, that it is only when the general constitution is lowered that the insidious onslaughts of micro-organisms are likely to prove successful. And thus when we glance at the causes which make patients liable to the disease, we

see what a great *rôle* debilitating agencies play, and how it becomes of the utmost importance, by the most careful scrutiny of the past, and of the family history, to check those agencies before they can do further harm. By such enquiries one is usually led to an offending organ or function, by the rectification of which, we, as far as possible, not only improve the general health, but prevent further infection.

We may now proceed to the consideration of the principles of treatment, as we understand them, dividing them into three sections: (I,) Diet, clothing, etc.; (II,) Drugs; (III,) Thermal, electric, and surgical treatment.

I.—Diet, Clothing, etc.

(a,) **Diet.**—No more fatal mistake can be made than to place a patient on what is popularly known as "low diet." This course was for years followed with disastrous results, in consequence of the belief that the disease was to a greater or lesser degree due to gout. Such we now know not to be the case, and the diet must, as far as possible, resemble that which one would recommend for that worst of all wasting diseases, namely, phthisis. Of course, where considerable febrile disturbance exists care must be taken to give suitable liquid nourishment until the febrile state has passed. With this proviso the diet should be of a nourishing, as well as of a mixed character. The practice of limiting the amount of nitrogenous food is not beneficial—in fact, as much nitrogenous food as can be digested should be given—care being taken to correct any functional derangement of the digestive organs. **Fats** are an important item, and above all in this class stands **cod-liver oil**, which should be regarded not as a medicine, but as a food, and should in conjunction with **maltine** be given at the termination of every meal. Of

vegetables, Spanish onion and celery are the best. **Stimulants** should be ordered, but not more than will stimulate the secretion of the gastric juice—malt liquors and good wines being preferred. Each individual case must be treated by itself, and no hard and fast rules can be laid down—the physician must exercise his own discretion. A good diet list is the following:—

May take Soups: Bouillon, mutton, chicken, oyster, turtle, barley, rice, bean, pea.

Fish: All that agree—boiled, baked, stewed or broiled.

Meats: Beef, broiled or roast; lamb, roast or broiled; mutton, roast or broiled; poultry, roast or broiled; game; sweetbreads; predigested meats (beef, peptonoids, sarco-peptones, peptonized beef-tea, essence of beef, beef jelly, etc.).

Eggs raw (and with whiskey, milk or sherry, sweetened), poached, boiled.

Fats and Oils: Mutton, beef, butter, olive oil, cod-liver oil.

Vegetables: Greens, lettuce, celery, spinach, asparagus, cresses, cauliflowers, onions, tomatoes, green peas, beans, lentils, and other leguminous vegetables; rice, well cooked, sparingly; radishes; potatoes, in their jackets, very sparingly.

Bread: Wheat and gluten bread, toast, milk toast. Bread should be at least one day old, and only a small quantity should be taken.

Fruits, Nuts, etc.: Oranges, lemons, pears, apricots, peaches, grapes, fresh figs, and dates; baked apples sparingly, and avoid them raw; walnuts, almonds, filberts, sparingly.

Drinks: Boiled water, Apollinaris and other carbonated waters, hot milk, cream, milk punch, egg-nog; peptonized milk, lemonade, ginger ale, sherbet; alcoholic drinks as prescribed (brandy, whiskey, wines, and malt liquors); malt preparations; coffee, cocoa, chocolate, tea sparingly and weak.

It is important to take food often and at regular intervals, care being taken that not more than three hours, except during sleep, passes without food. A glass of milk, or milk punch or liquid peptonoids, should be placed within easy reach in case of waking during the night.

During the day the following arrangements can be followed:—

7.30 a.m., and while still in bed, patient should have a cup of milk, with a dessert-spoonful of whiskey, brandy, or other stimulant, or with a small quantity of tea, cocoa, and a small piece of bread, toast, or biscuit.

8.30–9 a.m., breakfast of milk with a little tea, coffee or cocoa, toast or bread and butter, bacon, ham, fish, or eggs.

11 a.m., a tumblerful of milk, a cup of broth or beef-tea, or a sandwich, and a glass of wine.

1-1.30 p.m., a substantial meal of meat, poultry, fish, or game, with fresh vegetables, some light pudding or cooked fruit, and a glass of wine or malt liquor.

4 p.m., a glass of milk with a small quantity of tea, coffee, or cocoa, and some bread and butter or a plain biscuit.

7 p.m., another substantial meal similar to the mid-day one.

9.30-10 p.m., a cup of milk or bread and milk, or milk with some farinaceous food, such as Nestlé's, Mellin's, or Liebig's, etc.

(b,) **Clothing.**—The body must be encased in light woollen garments, worn if possible next the skin, care being taken not to over-clothe. A thin flannel vest and drawers with a piece of wash-leather inserted inside the fabric, next the skin, over the joints, is a most excellent plan. The feet must be carefully guarded, especially in damp weather. All undue exposure to damp and cold, it is needless to say, should be avoided, and the patient must be warned, if possible, not to expose himself during east and north-easterly winds.

(c,) **Exercise.**—During an acute attack, of course the patient should be confined to bed. As a rule this is unnecessary during the more chronic stages, a moderate amount of exercise being of advantage. If not able to walk, one should be careful to see that a sufficiency of fresh air, either by carriage-driving or in a Bath-chair is obtained. The use of carefully regulated and graduated gymnastics and special movements, passive exercises, the use of pulleys, weights, etc., are all of benefit.

II.—Drugs.

Almost every drug in the Pharmacopœia has at one time or another been used in this most intractable complaint, and all with more or less indifferent success. As these all, one after another, failed me, I turned to some of the newer drugs whose properties as antiseptics and eliminative agents appeared to promise success. After prolonged trial and experimenting, my results and deductions have led to certain facts being ascertained.

Treatment by drugs may be divided into three classes :—

A.—Those substances which when administered internally are antagonistic or antidotal to micro-organisms, or to their products, or which enter into conjunction with them and thereby assist in their elimination.

B.—Those substances (1) which act by improving the general tone of the organism, and help it to resist the inroads of micro-organisms ; and (2) those whose action is more or less indefinite, and which have been given empirically, and to relieve symptoms, and

C.—Those substances which are of use when applied externally.

A.—Those substances which are antagonistic or antidotal to the micro-organisms or to their products, or which enter into conjunction with them and thereby assist in their elimination.

In this group we have three sets of substances which from their nature give promise of benefit in rheumatoid arthritis. The drugs in each set enter into combination with various organic acids, and the resulting substances have all more or less direct antitoxic action. Their action varies in strength and efficiency according to the nature of their constituents. This is because their efficiency

depends on the rapidity of their decomposition after ingestion, and the rapidity of absorption after decomposition has occurred. Their primary action is undoubtedly a direct local one, and they, to a greater or lesser extent, counteract bacteria, and their products. After absorption they act more as eliminative substances entering into combination with the toxic albumens, thus favouring their elimination. The longer the substance takes to decompose the greater its local action, and, in inverse ratio, the greater the rapidity of decomposition the greater the rapidity of absorption and eliminative power.

The three sets of substances I have tried and experimented with are :—

1. The **creasotes** or **guaiacols** which enter into combination with carbonic acid yielding **creasotal, guaiacol carbonate,** and with benzoic acid yielding **benzosol.**

2. The **phenols** which enter into combination with salicylic acid yielding **salol** and **salophen** ; and

3. The **naphthols** which enter into combination with salicylic acid yielding **betol,** and with benzoyl chloride yielding **benzonaphthol.**

I have employed these substances largely in the treatment of this disease, and out of them all I have found a few of real use; the principal being those belonging to the creasote and phenol groups, probably from their quicker decomposition and greater eliminative powers. Those belonging to the naphthol group are practically unabsorbed, and act almost entirely locally. From my experience, I should say that it is the bases in all cases which are of use, and not the acids with which they combine. This is specially noticeable with the salicylic acid combinations, which instead of being the most useful, as one might fairly expect, are, except in the

case of salophen, the most useless. The following are of use: (1) Creasote; (2) Creasotal; (3) Guaiacol; (4) Guaiacol Carbonate; (5) Benzosol; (6) β-Naphthol; (7) Betol; (8) Salophen, and, to a less extent, (9) Salol.

My conclusions may be briefly summarised. The creasotes would appear to have a more or less specific action on the disease; whilst the phenols, with the exception of salophen, appear to be indifferent and useless; but the naphthols, by their intestinal action, apparently are of much use in a few cases.

The question now comes to be, How do the creasotes and their compounds act? It is supposed that they, their compounds and derivatives, have not, more than any other drug, any specific action on micro-organisms. According to Hudeod [1] they act not as antibacillary agents, but rather by setting up a substitutive irritation which successfully opposes the microbic inflammation. Dr. Douglas Powell [2] says that although creasote has little direct action, yet it has an indirect germicidal function. Others have stated that they act on the system generally, having no direct influence, by means of the stomach or by improving the general nutrition. They act locally, we know, on the alimentary canal before absorption, and afterwards by favouring the elimination of the toxic albumens with which they combine. Whilst in the gastro-intestinal tract they act on the mucous membrane as well as on the intestinal contents. As absorption proceeds their virtue as local antiseptics diminishes. It has been proved impossible to sterilize the blood, even after large doses (Hoelscher [3]), so it is by their secondary action that such drugs are more especially valuable. This may be so, but has it not been too readily assumed that these drugs have no direct action on the micro-organisms themselves? May they not to a great

extent impair their power to grow and multiply if they cannot actually destroy them? One of the arguments in favour of the disease being caused by micro-organisms, is this fact, that creasote and its allies are of use. To be of use, fortunately for suffering humanity, it is not necessary for a drug to destroy the micro-organisms but only to counteract their products, as all pernicious symptoms due to micro-organisms are produced by the deleterious effects of their products, and not simply by the mechanical presence of the bacteria themselves. It has been proved that the best antiseptics for the stomach are bismuth and charcoal; for the small intestine, salol, sodic salicylate or benzoate; and for the larger bowel, β-naphthol and charcoal (Bates[4]). β-naphthol has proved of special value, as on it the patient's general health has greatly improved, as well as the joint pains and swellings. Salol and betol appear to be less active than their bases, and they are not so remarkably useful as to encourage me in their further use.

1.—The Creasotes.

The creasotes are the drugs *par excellence* for rheumatoid arthritis, and without which one would feel helpless indeed, and one would drift back into that slough of despond in which for years those much in contact with this disease have been. Now, however, I hope a new era is dawning, and that at last we see a ray of light to lead us onward.

(a,) Creasote[5 to 11] (pure beechwood creasote) may be used in small doses, beginning with 2 drops and gradually increasing the dose to 15 or 20 drops, divided into three or four doses each. It may be given made up with alcohol, with some flavouring material, with cod-liver oil, or preferably in capsule. Creasote, although a complex body, has for its largest constituent guaiacol,

and to whose agency it owes most of its efficiency. It is strongly tasted, and has a most pungent odour. It is liable to cause nausea, gastric irritation, and to take away the appetite. Its use therefore is not unattended with difficulties.

(b,) **Creasotal** (Creasote Carbonate).—Through the union of creasote with carbonic acid we obtain a neutral material of a mild, oily taste, almost odourless, and non-caustic. It is as efficacious as creasote itself, and can be given in larger doses than the pure creasote. At ordinary temperature it is a thick fluid of an amber colour, soluble in alcohol, but insoluble in water. It may be given in doses of 15 to 20 drops daily.

(c,) **Guaiacol** [12] ($OH.C_6H_4.OC_3$), the principal constituent of creasote, has also a pungent taste and smell, and its administration is followed by the same drawbacks as that of creasote. Since the discovery of some of its compounds and derivatives, it has been less frequently used, but the benefit derived from its use is undoubted. It is best administered in capsules, or else dissolved in some form of tincture, in daily doses of ♏xx and over, and continued steadily for months. Should it not be bearable by the mouth, it may be administered hypodermically, as is recommended in phthisis by Dr. Picot,[13] of Bordeaux, and others. Administered thus it acts by reducing the temperature, causing a profuse sweating and allaying pain. Sciatica and supra-orbital neuralgia have been treated so with marked success by Anders.[20] He used ♏ij of guaiacol in ♏x of chloroform. Champonnière[21] used 10 centigramme doses dissolved in sterilized oil, and found it acted as a local anæsthetic as well as an analgesic. I have not, as a rule, found this hypodermic medication necessary. As an analgesic I always obtained success when applied externally, and, for its other properties, as its compounds are as active,

and are much more easily administered and assimilated, when given by the mouth, one usually prefers to use them.

(*d*,) **Guaiacol Carbonate** is an insoluble, tasteless, odourless, white crystalline powder. It has none of the unpleasant effects of creasote or guaiacol, which are so liable to irritate the stomach, and to destroy the appetite. It is slowly decomposed in the bowels, yielding guaiacol, which is absorbed into the blood, and carbonic acid. Within half to one hour after ingestion the guaiacol can be traced in the urine. It is by far the most useful of the whole series, but from its expense it has not been used so generally in hospital practice as it might have been. It is easily taken by the mouth either in powder, in pill, or in cachet. It is the drug on which I place most reliance, and in few cases have I found it ultimately to fail. It has now come to be my routine treatment, and I employ it in all cases, where active disease exists, in doses of grs. v—x, repeated three to four times daily. In no case have I seen any symptom of intolerance, nor have I noticed any evil effects produced.

Decomposition and absorption of the guaiacol carbonate takes place throughout the entire length of the small intestine. The process is a slow one. But the excretion of the guaiacol after it has reached the circulation is a rapid process. Frequently the urine shows the characteristic guaiacol reaction within half an hour after the ingestion of the drug; and the process continues for hours. The amount of guaiacol in the blood at any one time is small, and the action of the drug on the general system is a mild one, and cannot become dangerous even when the largest doses are given. The treatment of the disease is, therefore, a much more intensive one than with most other preparations, for a small quantity of

guaiacol is continually kept in the body fluids. The guaiacol leaves the body as an ethereal sulphate. Hence we may assume that during absorption the guaiacol combines with the albuminous elements of the blood, by means of the sulphur contained in the albumin molecules. This union of the guaiacol with the albumins takes place more especially with those of them that are distinguished by their chemical reactibility. These are of course the very poisonous albuminoids called the "labile albumins," which are caused by bacillary life action.

This union of the bacillary products with guaiacol is at once changed by the advent of oxygen. The guaiacol with the sulphur leaves the albuminous molecule, and the remainder undergoes further change, and these products are eliminated chiefly by the kidneys. Thus guaiacol carbonate unpoisons (if one may coin a word) the blood continuously. The body itself, freed from these poisons, regains its liberty to devote all its energy to the destruction of the micro-organisms.

(*e*,) **Benzosol** (Benzoyl-Guaiacol $C_{14}H_{12}O_3$), is a tasteless and odourless body which splits up into guaiacol, and benzoic acid in the digestive tract. It was introduced for use in phthisis by Dr. Walzer. It is insoluble in water, but is so in the gastro-intestinal tract, slightly in the stomach, but principally in the small intestines. It is very little soluble in glacial acetic acid, but is soluble in chloroform, ether, and hot alcohol. The dose is grs. vj, repeated three or four times a day. It is also of much use, but appears to be slightly less active than the carbonate.

Owing to the nauseous taste, disagreeable eructations, and gastric irritation set up by creasote and guaiacol, they are now seldom used internally. More often we use guaiacol carbonate and benzosol. The effect of any

one of the group is to improve the appetite, relieve pain, lower the temperature, stop all inflammatory process, and to improve the joint conditions. The patient sleeps better, gains flesh, pigmentation and other vaso-motor anomalies improve, the hands are no longer cold and dripping with perspiration, and the patient can move about with a great deal less pain, and more comfort. The patients' general appearance also undergoes change, they are no longer anæmic, anxious, and full of fancies, but say and look as if they were on the road to recovery. Of course such results are not obtained in a day, and are only brought about by the most careful combination of drugging and thermal treatment. With regard to the drugs, benzosol is often more immediately followed by relief of pain; but for long continued and severe cases, the carbonate is the more to be relied upon.

2.—The Phenols.

(*a*,) **Salophen,** a salicylic ether of acetylpara-amidophenol, contains 51 per cent. of salicylic acid. It is a crystalline, tasteless, odourless, white powder with a neutral reaction. It is insoluble in cold water, slightly so in hot, but dissolves readily in alkaline fluids and fairly well in alcohol and ether. It is not changed in the stomach, but in the intestines splits up into salicylic acid and acetylpora-amidophenol. Its advantages over salol are its freedom from taste and smell and its feebler toxic action.

(*b*,) **Salol** in a few instances, combined with salicylate of quinine, has given good results, especially in cases complicated by intestinal trouble. It is a valuable alternative drug, but cannot for routine treatment take the place of guaiacol.

Apart from their local action in the intestinal canal the phenols, like the guaiacols, form compounds with

toxic products in the blood and assist in their elimination.

3.—**The Naphthols.**

Betol, or Salicylate of β-naphthol, is a white, lustrous, crystalline powder nearly inodorous, insoluble in cold and hot water, soluble in boiling alcohol and in warm linseed oil, decomposes in the intestines into β-naphthol and salicylic acid. Betol is less active than β-naphthol itself, and has therefore nothing to recommend it. In all cases with intestinal disturbance, **β-Naphthol** is unrivalled, and its action is certain and safe. Given in v—x-grain doses the intestinal canal, if not rendered aseptic, is at least made less harmful, and the further absorption of deleterious products prevented. In about 5 per cent. of my hospital cases have I found it called for, and the result has always been most gratifying.

B.—Those substances which act by improving the general tone of the organism, and those whose action is more or less indefinite.

Of this class the principal drugs are **iron** and **arsenic.** It has not been stated even by the most ardent supporters of these drugs that they play any specific *rôle* in this disease. On the other hand, they have only been recommended as being those drugs which, from experience, have been found most useful in so improving the general health that the patient has been better able to withstand the inroads of the disease; and, as such, they are no doubt of great use. They are best administered combined with one another, either in the form of a pill or else in a mixture. The best preparation to use, of iron, is either the tincture of the perchloride, or the syrup of the iodide. Many prefer a preparation of iron and quinine, or of the ammoniated citrate. Arsenic may be given as the B.P. liquor, or as the liquor sodii arseniatis.

For the use of arsenic, we have the authority of Jenkinson, of Manchester, Beardsley, Charcot, Hilton Fagge,[14] etc. M. Noel Gueneau de Mussy recommended its use externally in the form of arsenical baths. Iron alone, or arsenic alone, is not nearly so successful as when the two are combined.

Iodine, and the various **iodides**, are commonly held to have a marked influence for good over the disease; iodide of iron being specially lauded as an agent of great value. Sir A. Garrod and Dr. A. E. Garrod [15] look upon this drug as the most efficient we possess. It is, however, probable that its usefulness depends mainly on the iron and not upon the iodide. Whether iodide of potassium, or even pure iodine, has any direct effect on the course of the disease it is difficult to prove or disprove, but, personally I have found little benefit from their use. If they do act they, probably, do so by virtue of their alterative or eliminative powers rather than by any direct action on the disease.

In a disease of such a nature it is no wonder we have a large list of drugs, which have, at one time or another, been recommended as sure and certain remedies. Of these the following are a few: the **alkalies, quinine, actæa racemosa, fraxinus excelsior, colchicum**, etc., which have been and still are recommended; but none of them are of any lasting avail. Some have found benefit from the use of the **salicylates**. Howard [16] says that if sodii salicylate is given in sufficient doses it promises well to be of more use, in the acute forms, or in the actively inflammatory periods and exacerbations, than any other form of agent. Including See's cases Compagnon [17] has related seventeen cases, in many of which the pain was relieved by its use, and its progress arrested. **Actæa racemosa**, according to Ringer, is of use in full doses, especially if the uterine functions are disturbed. **Guaia-**

cum has been recommended by many, and has occasionally been found of use. Lorenze and others mention **ichthyol**, but I have failed to obtain equally good results. For the relief of painful muscular cramps, Dr. Garrod uses **hyoscyamus**, with good results. Quite recently Solis-Cohen[24] has used an extract of thyroid glands and glycerine. The cases treated by him seemed to improve slowly. Hyde[25] recommends the use of extract of joints. I have tried this in a fairly large number of cases but have failed to obtain any encouraging results.

C.—Those substances which are of use when applied externally.

These substances have been used almost entirely for the relief of pain, and appear, except in the case of guaiacol, methyl salicylate, and carbolic acid applications, to have little other action. Every known form of counter-irritant has been tried, and of local applications there is practically no end. Much of the good experienced from their use has been the result of the friction and massage associated with their application. **Chili paste; turpentine; paraffin oil; camphor; ammonia; cajuput or eucalyptus oils; liniments of soap; ammonia; compound camphor; iodine; croton oil; turpentine; acetic turpentine or mustard;** have all been tried. Of local remedies for the relief of pain, the **liniments of chloroform, belladonna,** and **aconite** in equal parts applied on lint have often given ease. Dr. Spender paints a ring of **iodine** one-and-a-half inches wide above and below the joint. A **cantharides blister** may be tried on the proximal side of the joint. Flannel dusted over with **flowers of sulphur** is a popular remedy. **Chaulmoogra oil, cod-liver oil, oleate of mercury and morphine, unguentum-hydrarg. co.,** and others, have been used to rub into a joint, or for strapping. All have their advocates, and all are more or less inefficient. When articular pain is

severe, a local **vapour bath** or embedding the limb in **hot sand**, as recommended by Trousseau, may give relief. **Guaiacum plasters** in the more chronic stages have been known to relieve pain. With regard to this pain all the known hypnotics and analgesics have been at one time or another employed with more or less success. Should the local applications shortly to be mentioned not be successful we have to fall back on the use of **opium** or **morphia** in some of its forms, **paraldehyde, chloralose, sulphonal**, etc. Opium or morphia, as being the most certain, is preferable, and one often finds that after one or two good nights the use of the hypnotic is no longer required.

The external treatment I usually follow is, either to apply to the joints guaiacol and equal parts of olive oil; guaiacol in the proportion of one to six of tincture of iodine, methyl salicylate, pure or mixed with olive oil, or else warm carbolic acid fomentations. One not only gives great local relief, but, by absorption, the drugs have a beneficial effect on the disease itself. **Guaiacol** and **methyl salicylate**, when applied externally, produce a numbness, a sense of coolness and a feeling of relief. This effect becomes more marked with every application, and the joint condition often improves, simultaneously, in a most unexpected fashion. But the great thing is the relief of pain. Guaiacol was first used as an application to painful rheumatic joints by M. Desplats. He used equal parts of guaiacol and glycerine, and painted it on, covering it with a dry dressing. In three cases of arthritis deformans the results were excellent. To mask the odour, oil of cloves is the best according to Da Costa. Stolzeburg [18] says this treatment is accompanied by profuse sweats which it is unwise to continue for any length of time. I have never noticed these sweats. As a rule I apply it in equal parts with olive oil, or else with tincture of iodine, in varying propor-

tions, that of one to six being my most common one (iodine 6, guaiacol 1). It increases the flow of urine, and reduces the body temperature. Applied externally, according to Drs. Linossier and Lanois[19] it is absorbed rapidly, and can be easily detected in the urine. The body temperature has been known to fall as much as 2° after its application. Methyl salicylate, which must not be confounded with oil of wintergreen, may be applied pure as recommended by Sireday,[26] or else in varying proportions with olive oil, as used by Roger.[27] I usually use it at first in the proportion of 3 to 1 of olive oil and then pure. The preparation is applied to the skin and then covered with gutta percha tissue with a flannel bandage outside. Beyond a slight degree of redness it does not appear to produce any unpleasant effects, and its analgesic power compares favourably with that of guaiacol. **Carbolic acid** I use in the strength of 1 in 40, and apply it warm as a fomentation. This should be renewed every two or three hours. It acts much in the same way as guaiacol, reducing the temperature and acting as a local anæsthetic and analgesic. It is rapidly absorbed, as can be traced in the urine. It is not quite so efficient as guaiacol or methyl salicylate, but where the former cannot be used, on account of their odour, it is of use. It may also be tried with advantage in those cases where they are not very successful, as occasionally happens in acutely neurotic patients.

III.—Electrical, Thermal and other Special Modes of Treatment.

1. **Electrical Treatment.**—The weak continuous current (15 to 25 Leclanché cells), used twice a day, may be of service. The sponge electrodes being well moistened in hot salt and water, one is placed above the affected joint, and the other over the skin at any part of the limb

distal to the joint to be operated upon. Even the induced or interrupted current may be employed. I never use either during the acute stages, but later on when the disease has been subdued, and only weakness and atrophy remain, I have found great benefit, especially from the weak continuous current. Erb [22] treated a large number of cases by galvanism, and although having no absolute cures he had met with occasional good results, as far as improvement of the general state of nutrition, and of the local troubles were concerned. He considered it better to apply it direct to the spine than to the sympathetics. When the upper extremities are mainly affected, he passed the current through the cervical cord, and when the lower extremities are the principal offenders, the lumbar cord. It is recommended to continue the treatment for several months, but few patients will persevere with so prolonged a course. Dr. Steavenson and Dr. Garrod both mention the use of the electric bath. They consider that it exercises a favourable influence over the course of the disease. A bath tub is used of some non-conducting material, such as wood or porcelain, and this is filled with water at about the normal temperature of the body. A copper plate connected with the negative pole is placed at the foot of the bath, and a similar plate at the head is in connection with the positive pole. A galvanometer, measuring at least 250 milliampères, is used. The strength employed is about 200 milliampères, and it is computed that only 40 pass through the body, while the remainder pass through the water. The full current of 200 milliampères is used for about ten minutes. During the first six days the bath is given daily, and afterwards every second day.

2. **Thermal Treatment.**—Treatment by means of hot mineral waters, and other accessories, is of the greatest

value. To the consultant the choice of a suitable thermal water becomes of the first importance, but unfortunately no fixed rules can be laid down. In some cases the alkaline, or indifferent, and in others the sulphurous waters appear to answer best. Of the alkaline, or indifferent, **Bath** and **Buxton** in this country are the most frequented. Owing to its situation Bath is much warmer than Buxton in winter, and in the majority of cases is more suitable. In summer Buxton is preferred by many. Of the sulphurous **Strathpeffer** has latterly come to enjoy considerable repute as a summer resort, whilst **Harrogate** still maintains its ancient character for efficiency. Amongst the many other spas in this country are **Woodhall** (Iodine), in Lincolnshire, and **Llangammarch** (Bromine), in Wales, both of excellent service in certain cases; but for the average case the indifferent or alkaline waters are preferable. And of these, Bath maintains its premier position. Abroad we have the thermal waters of **Wildbad, Carlsbad, Wiesbaden, Töplitz, Homburg, Kissingen, St. Moritz, Bourboule, Mont D'Or, Aix-les-Bains, Hammam R'Hira, and Hammam Meskoutin, and Arkansas, Virginia,** and **Banff,** in America. When anæmia and debility are prominent symptoms, the chalybeate waters of **Langen Schwalbach, Rippolsau, Spa, Franzenbad,** etc., are of use. At **Aachen** special attention is paid to rheumatoid arthritis by means of douches and massage in conjunction with the general baths. Rademacker[23] has found great benefit from this plan of treatment, even in advanced cases.

The Bath thermal waters have been used for ages in this as well as in other joint complaints, and have come to possess a name and repute, for alleviating the symptoms of such disorders, second to none—in fact so much so that due discretion is not always observed either by the bathers or their medical advisers. Beyond all doubt

they are most useful in the early stages, and again when the disease is subdued they come to be almost equally invaluable. But no greater mistake can be made than to imagine that they will cure all and every condition. I hold that *alone*, during certain stages, they, like all other mineral waters, are not of the smallest use, but given a proper and successful medication we derive much help and good from them not only in alleviating symptoms, but in counteracting the effects of stiffness, deformity, and muscular weakness. I know of no waters, in this disease, of more avail than those of Bath. It has been said more than once that patients have derived no benefit from our waters, but so it may be said of any waters. Combined with suitable internal treatment, which must often be of a prolonged nature, no case should leave Bath unrelieved if not cured. But we must make it clear that once a joint is disorganised no power on earth can renew the diseased tissues. We may alleviate and relieve pain, give greater movement, and, in short, make life bearable, but we cannot make a joint quite perfect—there must always remain some symptoms to show how severe the attack has been. In severe and advanced cases improvement can only be obtained after months of treatment, a period often most trying both to the patient and the physician in charge. These facts should in all cases be laid before the patients and their friends to prevent disappointment and discouragement in protracted cases, which apparently make little progress, but which in the long run will usually yield to the means adopted for their amelioration. This I consider to be our duty not only to our patients but to ourselves as medical men.

At first, immersion in the Bath waters acts as a gentle counter-irritant—the gentle excitation of the cuticle being passed by reflex action throughout the body—an increased oxidation and production of heat being the

result. The circulation improves, and the tissues receive fresh supplies of blood to reinforce their vital powers. Again, wet and dry douching stimulates and exhilarates. The latter has to be used with care, as where the joints are sensitive it may do much harm. If practised as at Aix-les-Bains much benefit may be derived from it, however. In Bath this system has been carried to high perfection, where the attendants are not only highly qualified, but do their work with a thoroughness and care not often met with. The massage or shampooing combined with the douching has often a marvellous effect in the chronic stages. By its means the muscles are strengthened and further atrophy prevented, and it also seems to have a soothing effect on the joint pains and nerves. It is also of use in the insomnia which so often accompanies rheumatoid arthritis. When practised dry it appears to have a more exciting effect, and its results are not altogether so good. Massage again, where walking is difficult or impossible, keeps the muscles healthy and the skin in a condition of activity. It may be employed along with electricity, but certainly its best results are obtained when it is carried out in a bath by a skilful operator. When the attack is acute, only the lightest and slightest massage is permissible. As the joints stiffen it may become more forcible, and deeper, and should be combined with passive movements, under which treatment deformities and ankylosis often improve and do well.

In Bath we have one of the finest bathing establishments in existence, filled with all the necessaries and accessories so essential to the comfort of the invalid. Bathing may be carried out with or without the douche; douching with or without wet or dry massage; local vapour baths; specially prepared mud, medicated and electric baths; and baths and douches for special organs. The waters them-

selves are drunk not only on account of their constituents, but from the fact that they help to wash out impurities of the blood by flushing the kidneys; thus assisting the elimination of toxic products. The baths also act in a two-fold fashion, assisting the elimination of the toxic materials through the skin and lungs, as well as assisting in the improvement of the more purely mechanical defects.

Care must be taken not to push thermal treatment to such an extent as to debilitate the patient, and, therefore, it is probable that the course should cover a long period, with baths at considerable intervals, rather than a large number crowded into a short time.

Should it not be possible for a patient to go to a spa for treatment, as, alas! too many cannot, by careful bathing in an alkaline warm bath, much may be done at home. Massage and rubbing can usually be obtained anywhere, and gymnastics can be improvised. What answers well is a gentle course of gymnastics, pulleys, dumbells or elastic bands with handles, all of which if not carried too far are of much use.

Within the last few years, the **hot-air bath** has been used and found to be of much benefit, but only in the more chronic cases, and where the disease is not extensive.

Let us now for a moment glance at certain other methods and systems of treatment for special conditions. If pain, as we so often find it in the knees, be severe, and apparently from the rubbing of the ulcerated cartilages one upon another, the only method to deal with this is by **extension by weights.** Where fluid is exuded we seldom come across this difficulty, but now and again we see it, and are often puzzled as to the best means of subduing it. The weights should not be heavy, but should be applied continuously. Again, should there be an excess

of fluid present it may be desirable to **tap the joint**, and withdraw the fluid. I have often seen the mere fact of puncture relieve tension and give ease. One should not therefore be discouraged if no fluid is found. I find patients once relieved by this means ask for it to be done again and again. Should the jaws become either totally or partially **ankylosed** we are on the horns of a dilemma. If only partially ankylosed, probably a series of small blisters will relieve the difficulty (I never apply one larger than a shilling piece). Should it be unrelieved, we have to consider the advisability of **excision.** This has been done in several cases with fair success. It has also been practised on other joints, such as the knee or elbow, where there was little power and great crippling. In three cases I have seen the result, which was fairly successful in two. In both, there was before operation great deformity, and the limb was useless, not so much from pain as from inability to use it. In both, bony ankylosis ultimately resulted and there was no return of the disease in those joints. Of course the other joints remained *in statu quo ante.* In the other case, the pain and disease returned within a few months, probably from an insufficiently extensive operation. In a few cases I have recommended the operation as desirable, but in all it was declined. My personal knowledge therefore on this subject is slight. In Germany surgical treatment has recently become common, and successful results have been reported by, amongst others, Madelung,[28] Müller,[29] Felix Franke,[30] and Schüller.[31] In some of the cases reported by Schüller, after the excision of one joint, improvement followed in other affected joints.

Climate.—Whatever may be said, there can be no doubt that those who can afford it should not winter in this country. Egypt is *par excellence* the place for such to winter in. Biskra and some of the other Algerian

health resorts are nearly as good. What one has to bear in mind is that it is a dry warm atmosphere which is required, not a dry or a damp cold one. The northern Mediterranean sea-board, except during mild winters, and except in a few spots, is not advisable. It is better to live at home where all the comforts and necessities are so much better and more easily obtained. For those who have the time and money, a winter in the dry Karoo of South Africa is of advantage. I am not in favour of a long sea voyage, nor yet of residing near the sea. The moisture is invariably undesirable. A voyage often, by mere rest and absence of anxiety, may do wonders, but as routine treatment it is not advisable.

Such then is our armamentarium. Its constituents are numerous and various, but although many are interchangeable, yet each has its own peculiar mission for which it is best adapted. Every case must be carefully considered, from every point of view, thoroughly individualised, and the treatment best adapted to obtain the end in view firmly laid down and persisted with. A disease which has been gradually coming on for months, and of such a destructive character, cannot be expected to yield to a week or two of treatment, however skilfully devised or carefully carried out. Time is required, for it is not by any dexterous legerdemain, but by skilful application of remedies and by the steady accumulation of trifling advantages that we are finally enabled to subdue and overcome the enemy.

To summarise.—In the acute stages the patient should be kept in bed, on a light nutritive diet. The joints may be kept at rest, on a light splint, and painted with guaiacol and olive oil or iodine, or with methyl salicylate, or else fomented with carbolic acid solutions. Internally guaiacol carbonate or salophen should be given. If sleep is not readily obtained this must be attended to,

as must also be the gastro-intestinal and genito-urinary tracts. If the patient can stand it, light massage, and baths for short periods, as may be ordered. As it becomes more chronic the patient is allowed up, and the thermal treatment pushed—electricity and gymnastics often now being useful. The diet must be carefully supervised, the use of cod-liver oil and maltine being indicated. Internally, the treatment as in the acuter stages.

THE BATH THERMAL WATERS.

The springs which supply the waters of Bath are three in number, giving a daily yield of 507,600 gallons, at a temperature of 117–120° Fahr. If compared with other thermal waters of Europe and America, we see that those of Bath stand high in the scale.

EUROPE:

Germany,

	Fahr.
Aix-le-Chapelle (Kaiserquelle)	131·0°
Baden Baden (Hauptquelle)	155·4°
Ems (Kesselbrunnen)	118·4°
Karlsbad (Mülbrunnen)	136·0°
Karlsbad (Sprudel)	164·0°
Karlsbad (Schlorsbrunnen)	134·4°
Nuenahr (Mariensprudel)	101·7°
Schlangenbad	82·4°
Warmbrum	104·0°
Wiesbaden	105·6°
Wildbad	94·0°

France,

Aix-les-Bains	110·3°
Luchon	131·3°
Dax	140·0°
Monte Doré	105·8°
Barèges	111·0°

Italy,

Battaglia	160·0°

AUSTRO-HUNGARY,

Baden	96·8°
Töplitz (Hauptquelle)	120·0°
Gastein	87·0°

SWITZERLAND,

Leuk	123·0°

ENGLAND,

Bath	120·0°
Buxton	82·0°

AMERICA:

Hot Springs, Garland, Arkansas	93·0°–150·0°
Chalk Creek Hot Springs, Colorado	130·0°
Des Chutes „ „ Oregon	143°–145·0°
Madison Co. „ „ N. Carolina	102·0°

If compared with the waters of Buxton, those of Bath are seen to be much stronger :—

In an Imperial Gallon.	Bath.	Buxton.
Carbonate of Lime	9·001	9·185
„ Magnesia	0·399	4·746
„ Iron	1·217	0·037
„ Soda	15·017	...
Sulphate of Ammonium	...	0·014
„ Lime	69·984	0·673
„ Potash	6·702	0·678
„ Magnesia	35·042	...
„ Soda	23·140	0·202
Chloride of Sodium	17·894	4·517
„ Potassium	1·823	...
Silicate of Soda	0·399	...
Nitrite of Lime	1·562	0·266

In an Imperial Pint of the Bath Waters there is :—Oxygen 0·74 ; Nitrogen 4·60 ; Carbonic Acid 4·17 cubic inches.

The total amount of solids in each pint of the Bath waters is 168 grains. The amount of the gases, free and in combination,

is of the utmost importance, as they act as powerful stimulants by the excitation of the cuticle which they produce.

Compared with other waters we find the total amount of solids in each gallon to be :—

Kissingen	884·000
Marienbad	649·750
Baden	340·000
Karlsbad	496·071
Bath	**168·400**
Mont Doré	114·360
Töplitz	48·740
Warmbrunnen	40·380
Wildbad	35·870
Gastein	26·680
Römerbad	22·370
Buxton	20·579
Plombières	20·170

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CHAPTER VII.

SENILE ARTHRITIS.

Morbus Coxæ Senilis—Senile Arthritis—Monarticular Rheumatoid Arthritis—In whom seen—Symptoms—Morbid Anatomy—Changes in the Bones—Trophic Phenomena—Treatment.

Morbus coxæ senilis, senile arthritis, or, as many call it, **monarticular rheumatoid arthritis,** is most typically seen in the hip or shoulder joints of elderly people. It has been maintained, by some, that it is a similar condition to rheumatoid arthritis; but to this I cannot agree. For one thing it does not involve the peripheral joints, being confined almost entirely to the hips and shoulders. It is unaccompanied by any nerve or trophic phenomena, and the muscular wasting present is merely that induced by disuse, and mal-position of the bones. Taking it all round, it is quite distinct both clinically and pathologically. It is usually monarticular, but not invariably so, and, as I have said, principally affects the hips or shoulders. There is no symmetry, and it is most common in men—women more rarely being affected. It, as a rule, follows some injury of a very trifling nature, as with diseased arteries and tissues whose vitality is impaired it is possible, nay probable, that an injury will so affect the joint structures, both through their vascular and trophic supply, that a joint lesion may follow on what would otherwise be the most harmless incident.

Adams first gave to this disease the name of "Malum coxæ Senile," but later on substituted "Chronic Rheumatic Arthritis." Much has been written on the subject,

and, amongst others, we find Robert Smith,[1] Colles[2] and Wilmot[3] have done so with special reference to the disease as it occurs in the hip joints. Canton[4] refers to a similar condition in the shoulders, and Geist[5] describes the disease as a form of senile gout. Waldman[6] maintains that it is a separate disease from rheumatoid arthritis.

Symptoms.—As a rule, the disease begins as a gnawing pain, which speedily results in the loss of the use of the limb. If in the hip, the pain is often referred to the knee likewise, but, as a rule, the principal pain is felt over the trochanter or else in front in the groin. The pain is rarely, at first, so severe that the limb cannot be used, but, in the later stages, it may become marked. It is found the patient cannot cross the affected leg over the unaffected one without using his hands. There is inability to rotate the limb, and there is atrophy of the gluteal muscles, as well as of the muscles of the thigh. The tendon reflexes are increased. As the disease progresses we have considerable shortening, owing to absorption of the head of the bone. There may be eversion with some adduction. The movement of the joint is limited and attended with considerable pain, and distinct grating. Again, we may, occasionally, find cysts sometimes intimately in connection with the joint; but in others, at some distance from and free from it. They vary in size and are filled with thick, glutinous, straw-coloured fluid. As the progressive shortening of the limb proceeds, we have thickening of the trochanter, from the deposition of lime salts about its base, and it seems unduly prominent from the muscular wasting. The pelvis is often raised on the diseased side, as the patient, by introducing another joint, by walking on the toes, hopes to prevent shocks and jars to the diseased parts. The toes may be turned in or out,

but more usually the latter. The symptoms in the shoulder are somewhat similar. The arms cannot be raised from the side and any attempt to do so causes acute pain. When at rest the pain is not so acute as in the case of the hip. There is, however, a similar wasting of the muscles.

Post Mortem.—We find the joint distorted, the ligaments thickened, and the synovial membrane the seat of chronic inflammatory changes. The articulating surfaces are worn down—the cartilages being altogether destroyed or else still remain in patches, showing the bone here and there bare underneath. What remains of the cartilage can be easily stripped off, showing a rarefied condition of the bone. Instead of being hard and indurated, as one would find in the chronic stages of rheumatoid arthritis, we find it soft and yellowish in appearance, and it breaks down readily—apparently due to general wasting of the bone with fatty degeneration of the medullary substance. In the case of the hip, the neck may become so absorbed, that the head comes to rest on the trochanter. There may be an apparent widening of the acetabulum from the same reason. Occasionally there is true new bony formation around the neck, but this is rare. It may also occur round the articulating surfaces. The disease consists in a pure degeneration or wasting of the bone, followed by that of the cartilage. The changes in the bone are the primary and principal ones, those in the cartilages

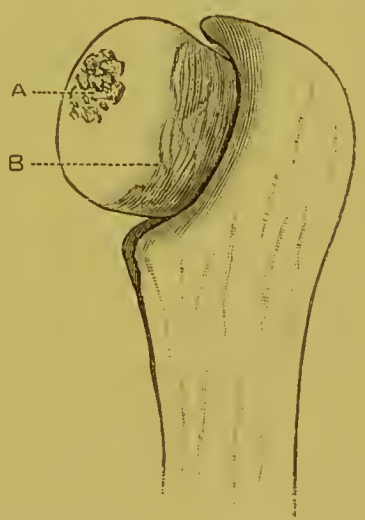

FIG. 9.—Head of femur from a case of Morbus Coxæ Senilis. A, ulceration, exposing softened bone, and B, neck greatly absorbed, with slight deposition of lime salts.

and synovial membrane being secondary. The bone is characterized by an increase in the number of its spaces; the trabeculæ are fewer in number; thinner and farther apart, and the spaces are filled with a yellowish marrow, consisting of round cells, granular corpuscles, and others having undergone fatty degeneration. It differs widely from the bone marrow in normal bone, and also from that found in true rheumatoid arthritis.

The disease appears, to me, to be a pure degeneration, due to some trophic or vascular malnutrition. With regard to treatment, nothing can be done beyond palliation. Relief of pain is our principal object, and is accomplished, more or less inefficiently, by the use of local applications, such as belladonna, small blisters, the continuous current, massage, bathing, etc. By good feeding, rest and stimulants, the progress of the disease for a time may be arrested, leaving only a permanent disorganization, which nothing can repair.

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APPENDIX.

For reference the report* furnished by Dr. Blaxall, of the British Institute of Preventative Medicine, on the micro-organisms found in Rheumatoid Arthritis by Dr. Wohlmann and myself, is herewith appended.

"THIS investigation was undertaken at the request of Dr. Bannatyne, of Bath, who stated that he, with Dr. Wohlmann, had arrived at the conclusion from the clinical aspect of cases suffering from rheumatoid arthritis, that the disease was due to a micro-organism, and further that by microscopic examination of the synovial fluid from affected joints, they had found an organism, constant and distinct, and this micro-organism they considered to be specific.

"Synovial fluid from affected joints was sent me from Bath the fluid was aspirated with antiseptic and aseptic precautions, with such success that out of eighteen cases which have been submitted to me, only twice have I found it contaminated.

"My first attempts to obtain organisms in the synovia and to obtain cultivations from it, resulted in failure. I adopted the ordinary methods of bacteriologieal procedure, staining films of the synovial fluid for a few minutes with aniline dyes, and inoculating serum tubes and all ordinary culture media, as well as making plate cultivations of nutrient agar-agar and gelatine after Koch's method. But I was unable to observe any organisms in the microscopic speeimens, or to recognize any appearance of growth upon any of the culture media.

"I then varied the staining methods, leaving the specimens in the dyes for a prolonged time in the cold, applying heat, and using concentrated solutions. By these means organisms

* This report appeared in the "Lancet," April 25th, 1896.

could be perceived in the specimens corresponding exactly to those described by Drs. Bannatyne and Wohlmann, and morphologically identical with those seen in their microscopic specimens. But their recognition was unsatisfactory, owing to several causes. In the first place, it was evident that the organisms took up the stains with great difficulty, and only by their prolonged action, or by the application of heat; but these means resulted in a very dense colouration of the synovial film. Secondly, they were decolourized with great ease, for attempts to decolourize the substratum left the organisms unstained.

"Again, the microbe being very minute, it was exceedingly difficult in heavily stained specimens to discriminate it from *débris* or from precipitate of the dye used. It was necessary then to find a method by which the organism should be well stained, should retain the stain, and yet allow the synovial film to be sufficiently decolourized, and one that should obviate all precipitate of the dye. I cannot claim to have attained this result, but after many trials I have adopted the following procedure as being most satisfactory.

"A thin film of synovial fluid, drawn out between two cover-glasses, is dried over the flame and fixed in the usual way, by passing through the flame five or six times, as otherwise the organisms are apt to be washed out. The cover-glass is then immersed in dilute acetic acid for about two minutes, well washed with water and dried again, this second drying being to prevent the cover-glass sinking in the staining fluid. The stain which I have found most useful is aniline methylene blue. The cover-glass is placed, specimen side down, on a watch-glassful of the stain, and the whole placed in a moist chamber in the dark, for three to five days. It is then washed in gently running water for some hours, rinsed in distilled water, dried and mounted in the usual way. More expeditious, though not giving such clear and well defined specimens, are aniline gentian violet and carbolic fuchsin. This latter stain I have found it advantageous to dilute one-third with distilled water. Twelve to thirty-six hours are

sufficient for these in a moist chamber. The cover-glasses are washed in running water in the same way, then well rinsed with thirty per cent. alcohol, washed in distilled water, dried and mounted. The acetic acid clears the synovial film and allows the dye to penetrate more readily. The prolonged staining deeply colours the organisms, so that the washing process leaves them well stained, though the film is decolourized ; and the moist chamber, by preventing the evaporation of the dye obviates the precipitate.

"Microscopic examination of the specimens reveals an organism possessing peculiar characteristics. At first-sight it appears to be a diplococcus, the two cocci being distinctly stained, but separated by a clear unstained interval—about equal in length to the diameter of either stained end. This interval I have never succeeded in staining. But careful observation will show, especially where the substratum is faintly coloured, that the intervening portion is nearly as broad as the diameter of either stained extremity, and that it has parallel contours. I therefore consider the organism to be a bacillus, which exhibits very marked polar staining. The average length is 2μ and the average breadth $\cdot 6\mu$, but this latter measurement varies greatly with the intensity of the staining. But the organism, as seen under the microscope, appears much smaller than the measurements would indicate, owing to the limited portions stained.

"The number of organisms met with in a cover-glass specimen of synovial fluid from a joint affected with rheumatoid arthritis varies greatly. Sometimes the field is crowded with them ; at other times they are scattered and hard to find. These differences appear to follow very closely the acuteness or chronicity of the disease.

"The organisms are generally evenly distributed through the film, showing, however, a tendency to congregate around the leucocytes. Their arrangement is always discrete ; I have never seen chains or masses formed.

"Though the staining methods mentioned above have given me the most satisfactory specimens, yet the organisms can be

seen when stained for a much shorter time, especially with gentian violet, methyl-violet, or carbolic fuchsin. But it is found that these stains if allowed to evaporate, deposit upon the cover-glass a precipitate of dye, which so closely resembles the organism, that it is by no means easy to recognize them when but few are present in a preparation so observed—because after such a brief staining, attempts to remove the precipitate by washing and the use of re-agents, bring about more or less completely the decolourization of the organism; whereas after a longer contact with the stain, the microbes are coloured more firmly, and are less easily decolourized. But there is one exception to this statement, in a method which I have devised and found useful.

"Impressed with the small size of the organism and the minute portion stained, it occurred to me that the protoplasm might take up dyes more readily if it came into contact with them while moist. With this in view I mixed a drop of synovial fluid with a few drops of the stain (aniline methylene blue being best) on a cover-glass, and rubbed out with a platinum needle. The cover-glass, with the stain and synovial fluid together, was then dried slowly over a burner, and when quite dry, fixed by passing several times through the flame, then freely washed with water, dried and mounted. In this way I obtained very fair results, the greater part of the stain being washed off, leaving the organism well coloured. For rapid diagnosis, this method is very useful.

"Treated by Gram's method, the organism is almost completely decolourized.

"I have been able also to detect the organism in the synovial fluid in the hanging drop specimen, but this is far from easy, unless they were present in larger numbers.

"I have now stained and examined the synovial fluid from various joints from eighteen cases affected with rheumatoid arthritis, and in every case have observed the organism which I have described above; but in fluids from distended joints, due to other causes, as chronic synovitis, gonorrhœal and tubercular affections, I have entirely failed to find them.

CULTIVATION.

"At first all attempts at cultivation, both aërobic and anaërobic, yielded apparently no result. But I imagined that this might be due in part to the small size of the organism, so that if it formed colonies they might be scarcely perceptible, and judging from the scattered distribution in synovia that the tendency to a free growth might be small, and in part to a slow development. Keeping these points in view I resolved to try it upon a large scale, and in such a manner, that any change in the medium might be easily detected. Into litre and half-litre flasks were put 250 ccs. of peptone beef-broth, filtered repeatedly until it presented a perfectly clear and bright appearance. Great care was taken over this to avoid the slightest obscuration. The flasks were sterilized and placed in an incubator kept at blood heat for several days to prove their sterility, and also to be sure that the fluid remained perfectly clear. If these conditions were fulfilled, the flasks were carefully opened, and a drop or two of synovial fluid from an affected joint allowed to enter. The flasks were then incubated at blood heat. Similar flasks, but uninoculated, were also incubated at the same time to serve as controls.

"I was fortunate enough to attain success with the first experiment. The first point noticed was that for three days the beef-broth remained perfectly clear, pointing strongly to the conclusion that the synovial fluid contained no ordinary organism. But, from the fourth day and onwards, there could be seen floating in the clear fluid very minute particles, and these increasing gave rise to an appearance resembling 'gold dust.' This effect was enhanced by lightly shaking the flask. Sometimes the growth seems to stop at this 'gold dust' stage, but at other times it may become slightly flocculent, recalling to mind the appearance of a commencing growth of tubercle bacilli in glycerine beef-broth. The beef-broth never becomes turbid, but always retains its bright appearance.

"The control flasks showed no such development. Micro-

scopic examination of such a culture, stained as before, displays the organisms in considerable numbers, but it can be readily understood from the delicate nature of the cultures and the imperfections of staining methods, that a too great reliance on stained specimens was not advisable, and that additional evidence would be helpful.

"Verification was obtained by making hanging drop specimens, and this is the easiest method of demonstrating the presence of the organism.

"In the hanging drop the microbe appears precisely as in the stained specimens, with two bright refractile ends, and an intermediate part much less obvious. They may occur in zoöglœa masses, or as discrete individuals hugging the edge of the drop. They are non-motile, but have a marked oscillatory movement. I have been fortunate enough to see them undergo division in the hanging drop specimen.

"The intervening portion lengthens out, the ends appearing to pull against one another energetically, and the whole organism oscillating the while uneasily. The middle part lengthens out more and more, so that the organism appears to be about twice its ordinary length; then suddenly the link snaps, and freed ends fly off in contrary directions, and are lost amidst their fellows.

"This phenomenon helps, I think, to explain some variations in length frequently noticed in stained specimens from culture. In these some bacilli will be seen very short, the stained ends quite close together, with a minute unstained connecting link, very suggestive of a diplococcus.

"These I take to be quite young organisms. Some, however, are much longer, attaining a length of 3μ, or possibly 4μ, the stained edges widely separated, and a clear unstained sheath faintly visible with the highest powers. These I imagine to be the older forms, soon about to divide. In these older forms too, the staining is sometimes somewhat different. Instead of the staining portion being more or less spherical at the ends of the organism, the coloured part is in the form of a conical cap, the base towards the centre of the bacillus,

and spreading faintly down the edges of the sheath. These forms show best the claim of the organism to be considered a bacillus. It will be obvious, however, that it is very difficult to bring out these subtle differences in a photograph—and indeed the limited staining of the organism and its minuteness, render the production of good photographs by no means easy.

"The organism also grows upon nutrient agar-agar. If beef-broth cultures are inoculated on tubes of sloping nutrient agar-agar, and incubated at blood heat, growth takes place in about three days, and in a very characteristic manner. This growth is exceedingly delicate. It appears no more than as a fine transparent film, which under a lens can be seen to consist of minute colonies no larger than a pin point, and perfectly transparent. To the naked eye it bears a very close resemblance to condensation water, though control tubes and the obvious tests show that this is not the case.

"It grows also in Löffler's serum, but here the growth is even more difficult to recognize, owing perhaps to the opalescence of the medium. It occurs as minute points, less difficult to observe at the lower part of the tube, where the condensation water has washed off the cholesterin. Stained cover-glass specimens, and hanging drop specimens made from such cultures, reveal an organism identical morphologically with that described as present in the beef-broth cultures and synovial fluid.

"I have also grown the organism in milk, where it appears to flourish, but without causing curdling, or precipitation of the casein. On nutrient gelatine, however, at 22° C., I have never succeeded in getting a growth, and in liquid gelatine incubated at 37° C. there is no visible growth.

"Examination of the blood in cases affected with rheumatoid arthritis has also afforded me positive results of the presence of the organism.

"I have examined the blood taken near to an affected joint, and also that from a distance, and in both have been able to detect the organism in microscopic specimens. Out of five

specimens of blood submitted to me, I have been successful in three, and these were the most severe cases. But further proof of the presence of the organism in the blood is the fact that twice I have been able to obtain cultures from it. The method was the same as previously described. The blood was inoculated into flasks of clear sterilized beef-broth and inoculated at blood heat temperature. Subcultures were also made from these flasks on to agar-agar and blood-serum. The organism found was identical in every respect with that which grew from the synovial fluid, and with that which was observed in the stained specimens.

"Some animal experiments have been made, for which I am indebted to the Council of the Royal College of Surgeons, and to Dr. J. Sims Woodhead Two ccms. were injected subcutaneously into mice, guinea-pigs, and rabbits, but without a fatal result. There is some reason to think, however, that the cultures set up a disease in rabbits, which affected the joints; but further experiments are necessary to arrive at the truth with regard to this matter.

"As far as I am aware only one organism has been previously associated with rheumatoid arthritis, which it is necessary to discuss. This was described by Schüller.* He writes of a bacillus 2·6μ long and ·75–·995μ broad, which exhibits polar staining. It is easily coloured by ordinary stains, especially carbolic fuchsin, but very easily decolourized. It is noteworthy that Schüller thinks it incumbent on him to point out the distinction between his organism and tubercle bacilli.

"It grows readily upon gelatine at 25° C. In two, three, or six days, small white grains or knobs appear. The gelatine is liquified, and eventually the organism grows to such an extent that the whole mass becomes opaque white. On agar-agar it grows as greyish white flecks or films.

"It is obvious that the organism described by Schüller

* Max Schüller: "Berliner Klinisch. Wochenschrift," September 4th, 1893.

differs markedly from the one under discussion. In fact the only points of resemblance are the polar staining and the easy discolourization. It therefore appears to me to be indisputable that this organism of Schüller's is not that which was discovered by Drs. Bannatyne and Wohlmann.

"To sum up:—

"(1,) In the synovial fluid in eighteen cases of rheumatoid arthritis an organism has been demonstrated, which is constant in its characteristics.

"(2,) The organism is a minute bacillus, exhibiting marked polar staining. It is difficult to stain and easily decolourized.

"(3,) The organism can be grown in culture media, and presents striking characteristics. In beef-broth it gives the appearance of gold dust; and on agar-agar and serum its growth is almost invisible.

"It does not grow on nutrient gelatine at ordinary temperature.

"(4,) It is present in the blood of severe cases.

"(5,) It has not been found in the synovial fluid from distended joints due to other causes.

"It should be added, that it has been impossible to examine sections of the synovial membrane, owing to the want of pathological specimens."

LIST OF AUTHORITIES.

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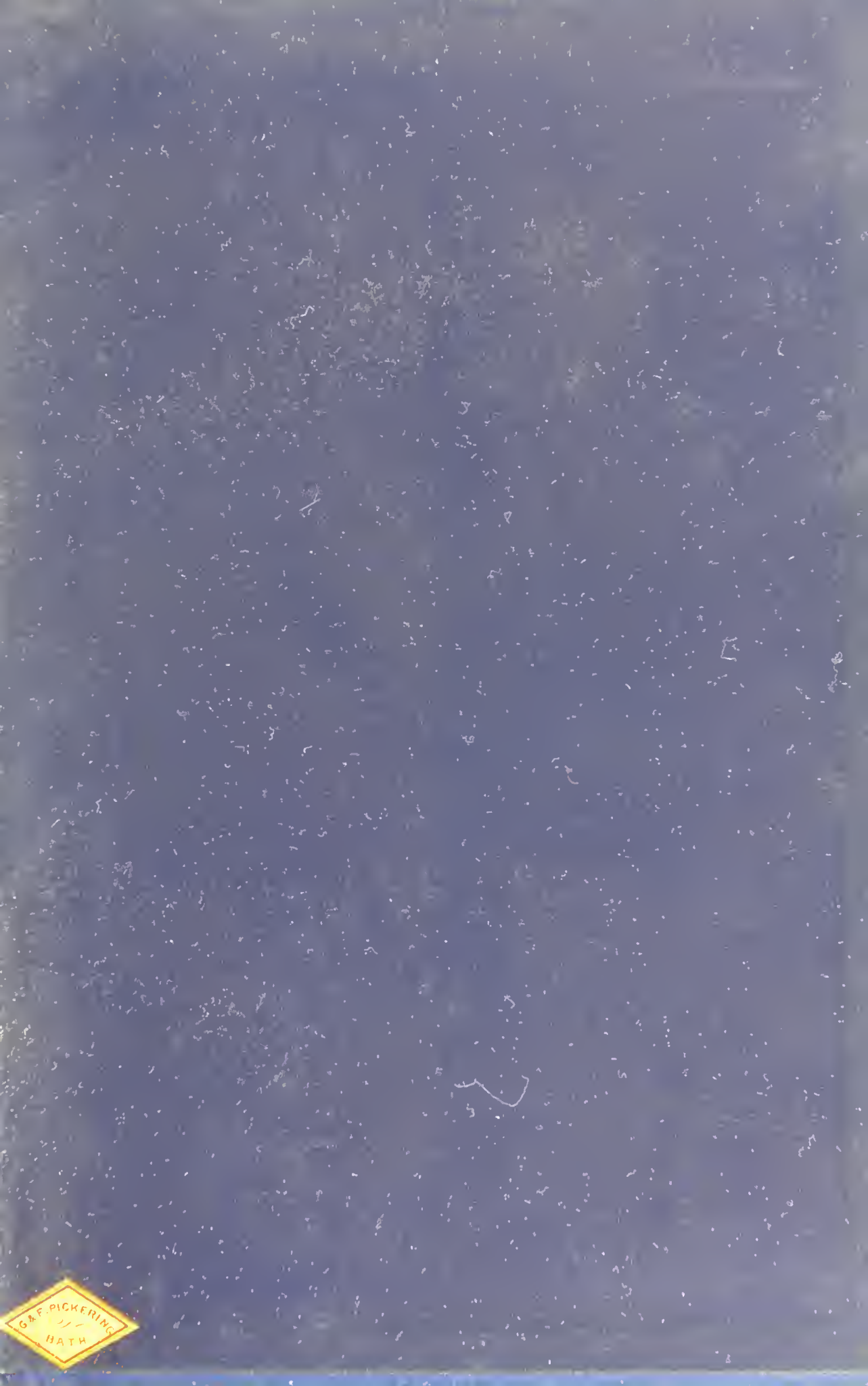
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